Opioid Treatment Program: Clinical Guidelines for methadone and buprenorphine treatment

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Functional Sub group Clinical/ Patient Services - Medical Treatment
Clinical/ Patient Services - Pharmaceutical
Population Health - Pharmaceutical
Summary To provide up to date policy and clinical practice guidelines in New South Wales for opioid treatment programs to treat heroin and other opioid dependence.

NOTE: Appendix V Guidelines and Information Sheets regarding Suboxone Sublingual Film was included in this Guideline on 31 August 2011 as advised by Information Bulletin IB2011_037.

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Audience Prescribers of opioid treatment, staff of drug treatment services
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New South Wales Opioid Treatment Program

Clinical guidelines for methadone and buprenorphine treatment of opioid dependence

Mental Health and Drug & Alcohol Office, NSW Department of Health

These guidelines are also available online at www.health.nsw.gov.au
## Quick contents

(Complete contents list is on page vi)

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Opioid dependence and treatment in New South Wales: summary</td>
<td>1</td>
</tr>
<tr>
<td>1.3 Rationale for methadone or buprenorphine treatment</td>
<td>2</td>
</tr>
<tr>
<td>1.6 Definition of opioid dependence</td>
<td>4</td>
</tr>
<tr>
<td>1.7 Treatment options</td>
<td>4</td>
</tr>
<tr>
<td>1.11 How opioid treatment is delivered in NSW</td>
<td>6</td>
</tr>
<tr>
<td>2 Clinical pharmacology: summary</td>
<td>8</td>
</tr>
<tr>
<td>2.1.1 Effects of opioids</td>
<td>10</td>
</tr>
<tr>
<td>2.1.2 Opioid withdrawal</td>
<td>11</td>
</tr>
<tr>
<td>2.2 Methadone pharmacology, side effects and drug interactions</td>
<td>11</td>
</tr>
<tr>
<td>2.3 Buprenorphine pharmacology, side effects and drug interactions</td>
<td>13</td>
</tr>
<tr>
<td>3 Entry into an opioid treatment program: summary</td>
<td>15</td>
</tr>
<tr>
<td>3.4 Key features of the initial assessment</td>
<td>18</td>
</tr>
<tr>
<td>3.5 Identifying opioid dependence</td>
<td>18</td>
</tr>
<tr>
<td>3.6 Indications for methadone or buprenorphine treatment</td>
<td>20</td>
</tr>
<tr>
<td>3.8 Contraindications to methadone or buprenorphine treatment</td>
<td>20</td>
</tr>
<tr>
<td>3.10 Relative merits of methadone and buprenorphine (choosing a treatment)</td>
<td>21</td>
</tr>
<tr>
<td>3.11.3 Special requirements for patients under 16 years of age</td>
<td>22</td>
</tr>
<tr>
<td>3.12 Elements required for informed consent to treatment</td>
<td>22</td>
</tr>
<tr>
<td>3.12.4 NSW Health’s required Treatment Agreement</td>
<td>24, 163</td>
</tr>
<tr>
<td>4 Commencing treatment: summary</td>
<td>25</td>
</tr>
<tr>
<td>4.2 Induction to treatment flowchart</td>
<td>29</td>
</tr>
<tr>
<td>4.4 Deciding on the starting dose</td>
<td>30</td>
</tr>
<tr>
<td>4.4.2.1 Transferring from methadone to buprenorphine</td>
<td>31</td>
</tr>
<tr>
<td>4.4.2.4 Transferring from buprenorphine to methadone</td>
<td>33</td>
</tr>
<tr>
<td>4.4.2.5 Transferring from naltrexone to buprenorphine or methadone</td>
<td>33</td>
</tr>
<tr>
<td>4.5.2.2 Titrating methadone dose</td>
<td>33</td>
</tr>
<tr>
<td>4.5.3.2 Titrating buprenorphine dose</td>
<td>34</td>
</tr>
<tr>
<td>4.7 Legal requirements for starting methadone or buprenorphine treatment</td>
<td>36</td>
</tr>
<tr>
<td>5 Continuing maintenance therapy: summary</td>
<td>39</td>
</tr>
<tr>
<td>5.1.1 Maintenance doses of methadone</td>
<td>40</td>
</tr>
<tr>
<td>5.1.2 Maintenance doses of buprenorphine (including less-than-daily dosing)</td>
<td>40</td>
</tr>
<tr>
<td>6 Takeaway doses: summary</td>
<td>45</td>
</tr>
<tr>
<td>6.1 Risks and benefits</td>
<td>47</td>
</tr>
<tr>
<td>6.4 Determining suitability for regular takeaway doses</td>
<td>48</td>
</tr>
<tr>
<td>6.4.1 Absolute contraindications to takeaway doses</td>
<td>48</td>
</tr>
<tr>
<td>6.5 Time in treatment and allowable takeaway doses</td>
<td>52</td>
</tr>
<tr>
<td>6.11 Lost or stolen takeaway doses and requests for replacement</td>
<td>54</td>
</tr>
</tbody>
</table>
### Specific Clinical Situations: Summary

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>55</td>
</tr>
<tr>
<td>7.1</td>
<td>62</td>
</tr>
<tr>
<td>7.2</td>
<td>63</td>
</tr>
<tr>
<td>7.3</td>
<td>64</td>
</tr>
<tr>
<td>7.4</td>
<td>66</td>
</tr>
<tr>
<td>7.5</td>
<td>67</td>
</tr>
<tr>
<td>7.8</td>
<td>69</td>
</tr>
<tr>
<td>7.10</td>
<td>70</td>
</tr>
<tr>
<td>7.11</td>
<td>73</td>
</tr>
<tr>
<td>7.12</td>
<td>74</td>
</tr>
<tr>
<td>7.13</td>
<td>76</td>
</tr>
<tr>
<td>7.15</td>
<td>77</td>
</tr>
<tr>
<td>7.17</td>
<td>78</td>
</tr>
<tr>
<td>7.18</td>
<td>78</td>
</tr>
<tr>
<td>7.26</td>
<td>81</td>
</tr>
<tr>
<td>7.27</td>
<td>81</td>
</tr>
</tbody>
</table>

### Ending Methadone or Buprenorphine Treatment: Summary

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>83</td>
</tr>
<tr>
<td>8.2.3</td>
<td>86</td>
</tr>
<tr>
<td>8.2.4</td>
<td>86</td>
</tr>
<tr>
<td>8.2.5</td>
<td>87</td>
</tr>
<tr>
<td>8.5</td>
<td>87</td>
</tr>
<tr>
<td>8.6</td>
<td>88</td>
</tr>
</tbody>
</table>

### Legal and Administrative Requirements: Summary

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>91</td>
</tr>
<tr>
<td>9.3</td>
<td>94</td>
</tr>
<tr>
<td>9.7</td>
<td>95</td>
</tr>
<tr>
<td>9.9</td>
<td>96</td>
</tr>
<tr>
<td>9.13</td>
<td>97</td>
</tr>
</tbody>
</table>

### Appendices

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>99</td>
</tr>
<tr>
<td>A</td>
<td>100</td>
</tr>
<tr>
<td>B, C</td>
<td>104</td>
</tr>
<tr>
<td>D</td>
<td>111</td>
</tr>
<tr>
<td>E</td>
<td>114</td>
</tr>
<tr>
<td>F</td>
<td>120</td>
</tr>
<tr>
<td>G</td>
<td>127</td>
</tr>
<tr>
<td>H</td>
<td>128</td>
</tr>
<tr>
<td>I</td>
<td>132</td>
</tr>
<tr>
<td>J</td>
<td>134</td>
</tr>
<tr>
<td>K</td>
<td>145</td>
</tr>
<tr>
<td>L</td>
<td>148</td>
</tr>
<tr>
<td>M</td>
<td>150</td>
</tr>
<tr>
<td>N</td>
<td>164</td>
</tr>
<tr>
<td>O</td>
<td>165</td>
</tr>
<tr>
<td>P</td>
<td>166</td>
</tr>
<tr>
<td>Q</td>
<td>169</td>
</tr>
<tr>
<td>R</td>
<td>170</td>
</tr>
<tr>
<td>S</td>
<td>171</td>
</tr>
<tr>
<td>T</td>
<td>173</td>
</tr>
<tr>
<td>U</td>
<td>174</td>
</tr>
</tbody>
</table>
New South Wales Opioid Treatment Program

Clinical guidelines for methadone and buprenorphine treatment of opioid dependence

Mental Health and Drug & Alcohol Office
NSW Department of Health

These guidelines are also available online at www.health.nsw.gov.au
Foreword


In reviewing these guidelines it was decided that there was value in increasing the scope of the document, and thus the new guidelines are larger and more detailed in many respects. The new guidelines also take account of the release of a buprenorphine plus naloxone combination, which has been designed to reduce risk of diversion of this product from patient use to street use.

The new guidelines are based on current literature, which indicates the cost efficiency of this approach to the treatment of opioid dependence. Both methadone and buprenorphine can lead to significant reductions in the adverse health, social and criminal consequences of opioid dependence and the guidelines seek to provide detail on the optimal use of these agents in the treatment of our patient population.

It is anticipated that these guidelines will be reviewed every two years by the Quality in Treatment Advisory Committee of the NSW Mental Health and Drug & Alcohol Office to ensure that they continue to reflect current best practice. As new agents become available in the treatment of opioid dependence (buprenorphine plus naloxone is the latest example and longer acting forms of naltrexone will be another), their use will be defined and information will be added to these guidelines.

The Committee preparing these guidelines has sought to ensure that all the literature relating to different methods for using these agents have been referred to in the text, and where possible, preferred methods of induction and maintenance care have been defined.

The electronic version of this document is available at <www.health.nsw.gov.au>.

It should be noted that in specific or unforeseen circumstances, clinicians may need to vary their clinical practice from that suggested in these guidelines. In such instances, clinicians should clearly document the reasons for such variations in the patient record. These guidelines should be used in conjunction with other national and state documents that relate to the use of methadone, buprenorphine and buprenorphine plus naloxone and that also deal with specific management situations, such as withdrawal management.
# Contents

**Foreword**

## 1 Opioid dependence and treatment in New South Wales

1.1 Introduction  
1.2 Types of opioid treatments  
1.3 Rationale for methadone or buprenorphine treatment  
  1.3.1 Buprenorphine–naloxone  
1.4 Purpose of this document  
  1.4.1 Previous clinical practice guidelines: methadone and buprenorphine  
1.5 Effectiveness of treatment for opioid dependence  
1.6 Characteristics of opioid dependence  
  1.6.1 ICD-10 description of dependency syndrome  
  1.6.2 Diagnostic criteria of opioid dependence (DSM-IV)  
1.7 Treatment options  
  1.7.1 Detoxification (withdrawal) programs  
  1.7.2 Naltrexone  
  1.7.3 Therapeutic communities (residential rehabilitation)  
  1.7.4 Self-help groups: Narcotics Anonymous  
  1.7.5 Counselling and support services  
  1.7.6 Drug courts and diversion program  
1.8 Case management and coordinated care  
1.9 Objectives of methadone or buprenorphine treatment  
1.10 Optimising the benefits of treatment  
1.11 How opioid treatment is delivered in NSW  
  1.11.1 Specialist clinics  
  1.11.2 Community pharmacies  
  1.11.3 General practitioners  
  1.11.4 Nurse practitioners  
  1.11.5 Public hospitals  
  1.11.6 Prisons and juvenile detention centres  
1.12 Social justice  

## 2 Clinical pharmacology

2.1 Basic opioid pharmacology  
  2.1.1 Effects of opioids  
  2.1.2 Opioid withdrawal  
2.2 Methadone  
  2.2.1 Side effects  
  2.2.2 Pharmacology and pharmacokinetics  
  2.2.3 Withdrawal  
  2.2.4 Drug interactions  
  2.2.5 Concurrent medical illness and methadone/buprenorphine  
2.3 Buprenorphine  
  2.3.1 Effects  
  2.3.2 Pharmacology and pharmacokinetics  
  2.3.3 Withdrawal  
  2.3.4 Drug interactions  
  2.3.5 Safety  
  2.3.6 Formulations  

## 3 Entry into an opioid treatment program

3.1 Assessing potential patients  
3.2 Building an effective therapeutic relationship  
3.3 Commencing harm reduction  
  3.3.1 Contraception  
3.4 Key features of the initial assessment  
3.5 Identifying opioid dependence  
  3.5.1 History  
    3.5.1.1 The typical day history  
    3.5.1.2 Overdose  
  3.5.2 Physical examination  
  3.5.3 Corroborative evidence  
  3.5.4 Urine tests  
3.6 Indications for methadone or buprenorphine treatment  
3.7 Specialist second opinion  
3.8 Contraindications to methadone or buprenorphine treatment  
3.9 Precautions  
3.10 Relative merits of methadone and buprenorphine  
3.11 Special patient groups  
  3.11.1 Priority patients  
  3.11.2 Patients aged 16–17 years  
  3.11.3 Patients aged under 16 years  
3.12 Informed consent and the treatment plan  
  3.12.1 Written information for the patient  
  3.12.2 Special warning: fitness to drive  
  3.12.3 Documenting the initial treatment plan  
  3.12.4 Treatment Agreement  
  3.12.5 Coordinating care and shared care  
  3.12.6 Release of information forms  
3.13 HIV, hepatitis B and hepatitis C screening
4 Commencing treatment

4.1 Induction to an opioid treatment program

4.1.1 Induction to methadone maintenance

4.1.2 Induction to buprenorphine maintenance

4.1.3 Induction and stabilisation: buprenorphine and methadone compared

4.1.4 Equivalence of buprenorphine and buprenorphine–naloxone

4.2 Induction to treatment flowchart

4.3 Treatment plan

4.4 Starting dose

4.4.1 Starting dose for new treatment

4.4.1.1 Starting dose of methadone — start low and go slow

4.4.1.2 Starting dose of buprenorphine

4.4.2 Starting dose when transferring from another treatment

4.4.2.1 Transferring from methadone to buprenorphine

4.4.2.2 Transferring from methadone to buprenorphine–naloxone

4.4.2.3 High-dose methadone to buprenorphine transfer

4.4.2.4 Transferring from buprenorphine to methadone

4.4.2.5 Transferring from naltrexone to buprenorphine or methadone

4.5 Stabilisation

4.5.1 Dose titration

4.5.2 Methadone

4.5.2.1 Monitoring during the first two weeks of treatment

4.5.2.2 Titrating methadone dose

4.5.3 Buprenorphine

4.5.3.1 Monitoring

4.5.3.2 Titrating buprenorphine dose

4.5.4 Dose titration after initial stabilisation

4.5.4.1 Methadone

4.5.4.2 Buprenorphine

4.6 Monitoring drug use

4.6.1 Self-report

4.6.2 Urine drug testing

4.6.3 Assessing alcohol abuse

4.7 Legal requirements for starting methadone or buprenorphine maintenance treatment

4.7.1 Identification

4.7.2 Authorisation

4.7.3 Prescriptions

4.7.3.1 Buprenorphine–naloxone prescriptions

4.8 Dosing location

4.8.1 Dosing at a clinic

4.8.2 Dosing at a pharmacy

5 Continuing maintenance therapy

5.1 Maintenance dose

5.1.1 Methadone maintenance

5.1.1.1 Upper limit of methadone maintenance doses

5.1.1.2 Split dosing

5.1.2 Buprenorphine maintenance

5.1.2.1 Maximum maintenance dose

5.1.2.2 Less-than-daily dosing

5.2 Treatment review

5.3 Case management

5.4 Maintaining health

5.4.1 General health issues in opioid dependent people

5.4.2 Alcohol and tobacco use

5.4.3 Other drug use

5.4.4 Psychosocial support

6 Takeaway doses

6.1 Risks and benefits of providing takeaway doses

6.2 Providing takeaway doses

6.3 Takeaway doses and buprenorphine

6.4 Determining suitability for regular takeaway doses

6.4.1 Absolute contraindications to takeaway doses

6.4.1.1 Repeated intoxication on presentation for dosing at the clinic/pharmacy

6.4.1.2 Child welfare issues/Department of Community Services involvement

6.4.1.3 Current chaotic and unpredictable behaviour

6.4.1.4 Assessed risk of self-harm

6.4.1.5 Current hazardous use of drugs

6.4.2 Determining stability — drug use indicators

6.4.2.1 Current drug use

6.4.2.2 Unstable drug use

6.4.2.3 Determining the level of drug use

6.4.3 Determining stability — psychosocial assessment

6.4.3.1 Attendance at regular clinic review appointments

6.4.3.2 Acceptable behaviour at prescriber practice and dosing site

6.5 Time in treatment and allowable takeaway doses

6.6 Monitoring patients on takeaway doses

6.7 When to stop providing takeaway doses

6.8 Takeaway dosing and the dosing schedule

6.9 Takeaway doses and transfer to another prescribing doctor

6.10 Authorisation, preparation, and supply of takeaway doses

6.11 Lost or stolen doses

6.11.1 Reporting lost doses
7 Specific clinical situations

7.1 Missed doses
7.1.1 Reintroducing methadone after missed doses 62
7.1.2 Reintroducing buprenorphine after missed doses 62
7.1.2.1 Procedure for patients receiving daily dosing 62
7.1.2.2 Procedure for patients receiving less frequent dosing 63

7.2 Vomited doses
7.2.1 Vomiting later than 20 minutes after consumption of methadone dose 63
7.2.2 Vomiting within 20 minutes of consumption of methadone dose 63
7.2.3 Pregnant patients who vomit a dose 63
7.2.4 Vomiting a buprenorphine dose 64

7.3 Managing polydrug use
7.3.1 Intoxicated presentation 64
7.3.2 Continued high risk drug use 64
7.3.3 Benzodiazepines 65
7.3.4 Selective detoxification 66

7.4 Overdose
7.4.1 Methadone 67
7.4.2 Buprenorphine 67

7.5 Incorrect dose administered
7.5.1 Preventing incorrect doses 67
7.5.2 Incorrect dose higher than the prescribed dose
7.5.2.1 Methadone 67
7.5.2.2 Buprenorphine 68

7.6 Use of high-dose methadone 68

7.7 High-dose buprenorphine 69

7.8 Managing difficult behaviour 69

7.9 Managing attempts to divert doses 69

7.10 Managing inpatients
7.10.1 Legal restrictions on prescribing drugs of addiction 70
7.10.2 Treatment of an inpatient currently on methadone or buprenorphine treatment 70
7.10.3 Patients with takeaway doses who are admitted to hospital 71
7.10.4 Acute pain management in hospital for patients on methadone or buprenorphine treatment 71
7.10.5 Responsibilities of the dosing location or prescriber 71
7.10.6 Treating opioid dependent inpatients not currently in an opioid treatment program
7.10.6.1 Methadone 72
7.10.6.2 Buprenorphine 72

7.11 Patients requiring pain relief
7.11.1 The opioid dependent person presenting with acute pain 73
7.11.2 Patients on methadone or buprenorphine treatment with acute pain 73
7.11.3 The opioid dependent person with chronic pain 73
7.11.4 The patient on methadone or buprenorphine treatment with chronic pain 73

7.12 Pregnancy and breastfeeding
7.12.1 Contraindication to buprenorphine in pregnancy 74
7.12.2 Contraindications to buprenorphine–naloxone in pregnancy and lactation 74
7.12.3 Methadone maintenance in pregnancy and breastfeeding 75
7.12.3.1 Starting methadone maintenance 75
7.12.3.2 Management in pregnancy 75
7.12.3.3 Dose reductions or detoxification during pregnancy 75
7.12.3.4 Breastfeeding 75

7.13 Neonatal withdrawal 76

7.14 Child protection 76

7.15 Consumption of methadone or buprenorphine by a child 77

7.16 Treatment of adolescents 77

7.17 Domestic violence 78

7.18 Patients with coexisting mental health problems 78

7.19 Patients with HIV 78

7.20 Patients with hepatitis B or C 78
7.20.1 Hepatitis B 78
7.20.2 Hepatitis C 79
7.20.3 Impaired liver function 79

7.21 Dosing arrangements for severely ill patients
7.21.1 Dosing at home 79
7.21.2 Collection of doses by a responsible carer 79

7.22 Multiple dosing locations 79

7.23 Gambling 80

7.24 Justice Health settings
7.24.1 Choice of methadone or buprenorphine in Justice Health settings 81

7.25 Patients under legal supervision 81

7.26 Urgent prescriptions due to unforeseen circumstances 81

7.27 Arrangements for travel 81
8 Ending methadone or buprenorphine treatment

8.1 Time in treatment 85

8.2 Planned withdrawal 85

8.2.1 The place for adjunctive pharmacotherapy during withdrawal 85

8.2.2 Avoiding secondary problems with alcohol and sedative/hypnotic drugs 86

8.2.3 Methadone dose reduction 86

8.2.4 Buprenorphine dose reduction 86

8.2.5 Transferring to naltrexone 87

8.2.5.1 Transferring from methadone 87

8.2.5.2 Transferring from buprenorphine 87

8.2.6 Transferring between methadone and buprenorphine 87

8.2.7 Readmission to treatment 87

8.3 Aftercare 87

8.4 Failure to attend for treatment 87

8.5 Involuntary withdrawal 87

8.5.1 Involuntary withdrawal from methadone 88

8.5.2 Involuntary withdrawal from buprenorphine 88

8.5.3 Complaints mechanism 88

8.6 Exiting and transferring patients 88

8.6.1 Treatment Exit Form 88

8.6.2 Transfer of dosing site 88

8.6.3 Transfer of information to new service provider 88

8.6.4 Refusal to exit a patient 89

9 Legal and administrative requirements

9.1 Legal and administrative framework for the Opioid Treatment Program 93

9.1.1 The Commonwealth Government Department of Health and Ageing 93

9.1.2 The NSW State Government 93

9.1.2.1 Enabling legislation 93

9.1.2.2 Mental Health and Drug & Alcohol Office (MHDAO)-93

9.1.2.3 Pharmaceutical Services Branch (PSB) of NSW Health 93

9.1.2.4 Justice Health 94

9.1.2.5 The Health Care Complaints Commission 94

9.1.2.6 The NSW Medical Board 94

9.1.2.7 The NSW Nurses and Midwives Board 94

9.1.3 Other bodies 94

9.1.3.1 The Methadone Advice and Complaints Service (MACS) 94

9.1.3.2 NSW Users and AIDS Association (NUAA) 94

9.1.3.3 The Coroner’s Court 94

9.2 The Pharmacotherapy Credentialling Subcommittee 94

9.3 Accreditation of prescribing doctors 94

10 Appendices

A Opioid withdrawal rating scales 100

B Methadone Syrup product information 104

C Biodone Forte product information 107

D Possible drug interactions with methadone 111

E Buprenorphine product information 114

F Buprenorphine–naloxone product information 120

G Possible drug interactions with buprenorphine or buprenorphine–naloxone 127

H Routine screening for domestic violence 128

I Intoxication and withdrawal states from commonly used drugs 132

J Assessment module for opioid treatment program induction 134

K Example of written patient information for induction to treatment 145

L Suitability for takeaway doses assessment form 148

M NSW Health forms used in the administration of the Opioid Treatment Program 150

N Example of a formal warning letter 164

O Patient identification 165

P Managing attempted buprenorphine diversion 166

Q Drugs of addiction (Schedule 8 of the NSW Poisons List) 169

R Patient consent form for buprenorphine treatment during pregnancy or breastfeeding 170

S Neonatal withdrawal scoring chart 171

T Guidelines for involuntary discharge 173

U Acknowledgements 174
# 1 Opioid dependence and treatment in New South Wales

<table>
<thead>
<tr>
<th>Chapter summary</th>
<th>See section</th>
</tr>
</thead>
<tbody>
<tr>
<td>Illicit opioid use has significant health, social and economic costs for individuals and Australian society.</td>
<td>1.1</td>
</tr>
<tr>
<td>This document provides clinical practice guidelines for opioid treatment in NSW to treat heroin and other opioid dependence.</td>
<td>1.4</td>
</tr>
<tr>
<td>There is extensive research evidence demonstrating the effectiveness of methadone and buprenorphine treatment of opioid dependence.</td>
<td>1.5</td>
</tr>
<tr>
<td>Opioid dependence is characterised by a strong desire to take the drug, difficulties in controlling its use, persisting in use despite harmful consequences, giving a higher priority to drug use than other activity and obligations, increased tolerance, and physical symptoms when the drug is withdrawn.</td>
<td>1.6</td>
</tr>
<tr>
<td>A range of treatments for opioid dependence, other than methadone or buprenorphine, are available that may suit different individuals:</td>
<td>1.7.1</td>
</tr>
<tr>
<td>• withdrawal management (“detoxification”)</td>
<td>1.7.2</td>
</tr>
<tr>
<td>• naltrexone</td>
<td>1.7.3</td>
</tr>
<tr>
<td>• therapeutic communities (residential treatment)</td>
<td>1.7.4</td>
</tr>
<tr>
<td>• self-help groups: Narcotics Anonymous</td>
<td>1.7.5</td>
</tr>
<tr>
<td>• counselling and support services</td>
<td>1.7.6</td>
</tr>
<tr>
<td>• drug courts and diversion program.</td>
<td>1.8</td>
</tr>
<tr>
<td>Case management and coordinated care are strongly recommended. In this approach, one clinical person is identified as the case manager who regularly monitors the patient, and coordinates care when multiple professionals are involved in treatment.</td>
<td>1.9</td>
</tr>
<tr>
<td>The aims of an opioid treatment program are to:</td>
<td>1.10</td>
</tr>
<tr>
<td>• reduce or eliminate heroin and other illicit drug use by those in treatment</td>
<td>1.11.1</td>
</tr>
<tr>
<td>• improve the health, psychological functioning and wellbeing of individuals and families</td>
<td>1.11.2</td>
</tr>
<tr>
<td>• facilitate the social rehabilitation of those in treatment</td>
<td>1.11.3</td>
</tr>
<tr>
<td>• reduce the spread of bloodborne diseases associated with injecting opioid use</td>
<td>1.11.4</td>
</tr>
<tr>
<td>• reduce the risk of overdoses and deaths associated with opioid use</td>
<td>1.11.5</td>
</tr>
<tr>
<td>• reduce the level of involvement in crime associated with opioid use.</td>
<td>1.11.6</td>
</tr>
<tr>
<td>The benefits of treatment are optimised when programs are readily accessible, entry into treatment is prompt and retention in treatment is high. Outcomes improve as time in treatment increases.</td>
<td>1.12</td>
</tr>
<tr>
<td>Treatment is delivered in NSW via:</td>
<td>1.13</td>
</tr>
<tr>
<td>• specialist clinics</td>
<td>1.13.1</td>
</tr>
<tr>
<td>• community pharmacies</td>
<td>1.13.2</td>
</tr>
<tr>
<td>• general practitioners</td>
<td>1.13.3</td>
</tr>
<tr>
<td>• nurse practitioners</td>
<td>1.13.4</td>
</tr>
<tr>
<td>• public hospitals</td>
<td>1.13.5</td>
</tr>
<tr>
<td>• prisons and juvenile detention centres.</td>
<td>1.13.6</td>
</tr>
<tr>
<td>The Opioid Treatment Program in NSW direct particular attention to subgroups of illicit drug users with special needs and among whom health status reflects some disadvantage.</td>
<td>1.14</td>
</tr>
</tbody>
</table>
1.1 Introduction

The health, social and economic costs of heroin and other illicit opioid use are significant for individuals and Australian society. The costs of heroin include a wide range of adverse outcomes such as overdose deaths, spread of infectious diseases (particularly HIV/AIDS, hepatitis B and C), other medical and psychological complications, social and family disruption, harm to the welfare of children, violence and drug-related crime and problems associated with the black market economy and corruption.

Providing a range of accessible and effective treatments for heroin and other illicit opioid use such as methadone or buprenorphine treatment (opioid replacement therapies or pharmacotherapies) can reduce demand for illicit drugs and minimise the adverse consequences.

Since the NSW Drug Summit in 1999 there has been a significant expansion of the methadone program, more active case management and the introduction of alternative treatments like buprenorphine.

Further information

1.2 Types of opioid treatments

The class of drugs known as opioids includes opium, codeine, oxycodone, morphine, diacetylmorphine (heroin), pethidine, methadone and buprenorphine.

The main types of opioid treatment available in NSW are:

- methadone, which is available in two preparations (Methadone Syrup® and Biodone Forte®)
- buprenorphine (Subutex®)
- buprenorphine plus naloxone (Suboxone®).

Relapse prevention treatment using naltrexone (ReVia®) is also available.

1.3 Rationale for methadone or buprenorphine treatment

Dependence on heroin and other opioid drugs develops from initial experimental and recreational use to more intensive and compulsive use, often daily. Opioid dependent people spend increasing amounts of time, money and energy in seeking and taking drugs, and their health, work and personal relationships deteriorate as a result. Pressure to maintain a heroin habit and an increasing preoccupation with drug seeking and drug use often come to dominate a person’s life.

Many opioid dependent people have a background of social disadvantage, disrupted early relationships, and a history of problems in adjustment and relationships. Opioid dependence compounds these problems. Clinical research in Australia and overseas shows that methadone or buprenorphine treatment is effective in reducing heroin use, in reducing the risk of death by overdose, in freeing people to engage in normal activities, and in reducing crime associated with drug use.

Once established, opioid dependence is a chronic, relapsing condition, and most opioid users who attempt withdrawal rapidly lapse back into drug use. Methadone and buprenorphine maintenance are long-term treatments, and there is strong and consistent evidence that longer periods of treatment are associated with better outcomes.

Treatment with methadone or buprenorphine helps to normalise the life of drug users due to the pharmacological properties of these drugs. Methadone and buprenorphine are slowly absorbed and have a long duration of action. People maintained on a single daily dose reach blood levels of methadone or buprenorphine that fluctuate in a relatively narrow range. People become tolerant to the effects of this stable blood level, so that maintenance treatment produces very few symptoms of intoxication or withdrawal. This is the process of stabilisation — the production of a state in which intoxication and withdrawal are minimised.

By inducing tolerance to opioid effects, methadone and buprenorphine blunt the response to administered heroin, so that heroin use ceases to reinforce the drug habit. By blocking the effects of heroin, and stabilising withdrawal symptoms, high doses of methadone or buprenorphine are highly effective in suppressing heroin use. Almost all the benefits of methadone or buprenorphine treatment — reduced crime, reduced risk of bloodborne virus infections, improved social functioning — result from reduced heroin use.

Participation in methadone or buprenorphine treatment brings many previously marginalised heroin users into contact with health services. Psychiatric and medical problems, relationship difficulties, and problems in accessing welfare services are common in this population. Access to health services, counselling, and welfare services are facilitated through participation in the treatment program.

1.3.1 Buprenorphine–naloxone

The development of the combination product of buprenorphine plus naloxone (Suboxone®) in a 4:1 ratio was prompted by concerns over the abuse potential of buprenorphine. The addition of naloxone, which is poorly absorbed via the sublingual or oral route, is designed to make the product less likely to be diverted and injected.

Buprenorphine plus naloxone will be available for patients on buprenorphine who are assessed as being suitable for take-away doses or, ultimately, treatment without direct supervi-
sion of administration. This is expected to represent between 10%–20% of people currently in treatment. Eligible patients will be switched from buprenorphine (Subutex®) to the combination product, and provided with progressively more doses to take without direct supervision, with some (a minority) reaching the stage of picking up medication monthly.

The focus of these guidelines is on clinical assessment and the process by which patients can be appropriately selected to receive takeaway (unsupervised) doses of medication.

A decision to provide unsupervised doses to a patient is founded on the prescriber’s informed clinical judgement that:

- the medication will be taken as directed by the person who receives the prescription
- providing such doses will enhance the wellbeing of the patient
- reduced levels of supervision will not destabilise the patient
- providing takeaway doses will not increase the risk to the community or degrade the integrity of treatment services.

The introduction of buprenorphine–naloxone should be used as an opportunity to increase the transparency of clinical decision-making processes within the Opioid Treatment Program. Information sheets on buprenorphine–naloxone will be produced for patients, explaining how decisions will be made concerning the provision of unsupervised doses. Patients should be encouraged to help their prescriber obtain adequate evidence to support provision of unsupervised dosing. Attention should be focussed on getting patients to be active partners in their treatment program and evaluation (eg, in providing urine samples).

1.4 Purpose of this document

The purpose of this document is to provide up to date clinical practice guidelines in NSW for opioid treatment of heroin and other opioid dependence.

1.4.1 Previous clinical practice guidelines: methadone and buprenorphine

This document amalgamates and replaces two previous NSW Department of Health documents:

- New South Wales methadone maintenance treatment clinical practice guidelines (NSW Health, 1999)

The document also incorporates policy and procedures developed through the National Drug Strategy.

1.5 Effectiveness of treatment for opioid dependence

There is extensive research evidence demonstrating the effectiveness of opioid replacement therapies (Ward, Mattick and Hall, 1998). A review by the Australian National Council on Drugs (ANCD) rated the evidence as strong for methadone, and moderate for buprenorphine. Evidence for the efficacy of naltrexone in relapse prevention treatment is limited (Gowing et al, 2001, Tucker et al, 2004).

The National evaluation of pharmacotherapies for opioid dependence (NEPOD) compared methadone, buprenorphine and naltrexone and concluded that methadone maintenance is the most cost-effective treatment currently available in Australia for treatment of opioid dependence (Mattick et al, 2004: 5). This may reflect the fact that most experience has been gained with methadone maintenance treatment, which was introduced to Australia in 1969.

The challenge for clinicians is to determine the most suitable treatment for opioid dependent individuals. These guidelines will assist clinicians in matching and managing individuals to the most appropriate treatment.

Evidence of effectiveness of treatment


1.6 Characteristics of opioid dependence

Dependence on heroin and other opioid drugs develops over time from initial experimental and recreational use to more intensive and compulsive use, usually daily. Once dependence on heroin is well established it becomes a chronic relapsing condition.

Opioid dependence is defined below according to the International Statistical Classification of Diseases and Related Health Problems (ICD-10) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV).

1.6.1 ICD-10 description of dependency syndrome

The ICD-10 description of the dependency syndrome is:

A cluster of behavioural, cognitive, and physiological phenomena that develop after repeated substance use and that typically include a strong desire to take the drug, difficulties in controlling its use, persisting in its use despite harmful consequences, a higher priority given to drug use than to other activity and obligations, increased tolerance, and sometimes a physical withdrawal state.

1.6.2 Diagnostic criteria of opioid dependence (DSM-IV)

A maladaptive pattern of substance use leading to clinically significant impairment or distress as manifested by three or more of the following occurring at any time in the same 12-month period.

1 Tolerance, as defined by either of the following:
   • a need for markedly increased amounts of opioids to achieve intoxication or desired effect
   • markedly diminished effect with continued use of the same amount of opioids.

2 Withdrawal as manifested by either of the following:
   • the characteristic withdrawal syndrome for opioids
   • opioids or a closely related substance are taken to relieve or avoid withdrawal symptoms.

3 Impaired control over use: Opioids are often taken in larger amounts or over a longer period than was intended.

4 Wish to quit: There is a persistent desire or unsuccessful attempts to cut down or control opioid use.

5 Time lost to drug activities: A great deal of time is spent in activities necessary to obtain opioids, use opioids, or recover from their effects.

6 Lifestyle changes: Important social, occupational, or recreational activities are given up or reduced because of opioid use.

7 Consciousness of drug use being out of control: The opioid use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by opioids.

1.7 Treatment options

In the past decade there have been significant advances in the treatment of heroin and other opioid dependence. Although the emphasis in this document is to provide evidence-based best practice guidelines on methadone and buprenorphine treatment, it is important to consider other treatments that may be more suitable for some individuals.

The treatments listed below are not mutually exclusive. Most opioid dependent people will undergo several episodes of various treatments or be involved in multiple services at any one time.

1.7.1 Detoxification (withdrawal) programs

Drug withdrawal management, commonly called detoxification, can be conducted in inpatient and/or outpatient settings. Withdrawal from heroin and other short-acting opioids takes approximately 5 to 7 days, longer for methadone. Buprenorphine is commonly used for medicated withdrawal management.

Although a range of health benefits are often derived from detoxification, detoxification alone leads to lasting abstinence from drugs or significantly improved health and functioning for only a small minority of patients.

Further information

New South Wales clinical practice guidelines for managing drug withdrawal. (Forthcoming.)
1.7.2 Naltrexone

Naltrexone, a long-acting, highly specific opioid antagonist, blocks opioid receptors so that the patient does not experience the usual effects of taking opioids. It competitively displaces opioid agonists if they are present. A small group of patients who are committed to achieving abstinence may benefit from naltrexone maintenance treatment.

1.7.3 Therapeutic communities (residential rehabilitation)

Residential rehabilitation programs in therapeutic communities range from 1 to 12 months. Programs vary in structure and the range of interventions offered.

1.7.4 Self-help groups: Narcotics Anonymous

The best known self-help group for former illicit drug users is Narcotics Anonymous (NA), which is based on the 12-Step Program developed by Alcoholics Anonymous (AA).

1.7.5 Counselling and support services

Counselling and support services refer to the wide range of programs and services (often called psychosocial interventions) including individual counselling, group therapy, cognitive-behavioural therapy, relapse prevention, motivational interviewing, mental health interventions, as well as support for employment, accommodation, children, financial, legal and other problems.

1.7.6 Drug courts and diversion program

Drug courts and diversion programs have increased rapidly in Australia and overseas. The aim is to divert individuals with drug problems from the criminal justice system to treatment and rehabilitation. Such diversion programs use one or more of the treatment options outlined above.

1.8 Case management and coordinated care

For some opioid dependent people, methadone or buprenorphine maintenance is all that is required for effective treatment. Others have difficulties in relationships, psychiatric problems, or other issues which mean that much more is needed to achieve good treatment outcomes. To ensure that patients are receiving care adequate to their needs, all people stabilised on methadone or buprenorphine require comprehensive assessment and identification of treatment issues, followed up with periodic monitoring and review to reassess their situation.

In fostering social reintegration of people whose lives are dominated by heroin addiction, treatment comprises a blend of support and structure. “Support” involves the establishing a safe and non-judgmental therapeutic environment and a respectful and tolerant therapeutic relationship. “Structure” refers to the rules of treatment — such as requirements for supervised dosing, behavioural expectations (such as not tolerating abuse or threats to staff or to other patients), and attendance for review interviews.

To provide a blend of support and structure, a “case management” approach to treatment is strongly recommended. In this approach, one clinical person — the “case manager” (sometimes referred to as “key worker”) is identified as the person who regularly monitors the patient, and coordinates care when multiple professionals are involved in treatment.

For people receiving methadone or buprenorphine in primary care settings, the case manager will usually be the prescriber, who monitors the patients with regular reviews. The case manager in a specialist clinic may be the prescriber or some other person (eg, social worker, nurse or counsellor) who liaises with prescribers over management decisions.

The case manager should be identified in the patient’s medical record. Having a case manager ensures continuity and coordination of care, and fosters the establishment of a therapeutic relationship. It also minimises the risk of patients playing health professionals off against each other.

The case manager coordinates treatment according to the treatment plan documented in the medical record (see section 3.12.3, Documenting the initial treatment plan, on page 23, and section 4.3, Treatment plan, on page 30).

Further information


Further information on alternative treatments


Further information


1.9 Objectives of methadone or buprenorphine treatment

The aims of methadone or buprenorphine treatment are to:

- reduce or eliminate heroin and other illicit drug use by those in treatment
- improve the health, psychological functioning and well-being of individuals and families
- facilitate the social rehabilitation of those in treatment
- reduce the spread of bloodborne diseases associated with injecting opioid use
- reduce the risk of overdoses and deaths associated with opioid use
- reduce the level of involvement in crime associated with opioid use.

1.10 Optimising the benefits of treatment

The benefits of opioid treatment are optimised when programs are readily accessible, entry into treatment is prompt and retention in treatment is high.

Outcomes improve as time in treatment increases. Patients should be encouraged to remain in treatment for at least 12 months to achieve enduring lifestyle changes. People who drop out of treatment, particularly in the first year, are highly likely to return to opioid use, criminal activity and social dysfunction.

Factors that maximise participation in opioid treatment include:

- ease of access
- affordability
- flexible opening hours at clinics
- adequate doses
- non-judgemental clinicians
- high staff morale
- good patient–clinician relationships
- access to allied medical, psychological and welfare services.

1.11 How opioid treatment is delivered in NSW

Treatment is most commonly provided through outpatient clinics (public or private), community pharmacies and local hospitals, particularly in rural areas. Prescribers can be either public (career medical officers, registrars, drug and alcohol staff specialists, drug and alcohol nurse practitioners and visiting medical officers) or private (general practitioners, drug and alcohol nurse practitioners and psychiatrists).

1.11.1 Specialist clinics

Specialised opioid treatment program clinics, sometimes called pharmacotherapy units, can be private or public. They generally have the capacity to provide services to a large number of clients. Clinics are typically multidisciplinary and staffed by authorised prescribers, dosing staff (usually registered nurses and enrolled nurses), and allied health workers.

1.11.2 Community pharmacies

Community or retail pharmacies can provide methadone and buprenorphine dosing. The number of patients varies from less than 5 up to 50. In many rural areas, community pharmacies are the only dosing points available.

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**NSW Opioid Treatment Program (OTP)**

<table>
<thead>
<tr>
<th>Dosing points</th>
<th>Prescribers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Public OTP clinics</strong></td>
<td></td>
</tr>
<tr>
<td>Public hospitals</td>
<td>Public patients</td>
</tr>
<tr>
<td>Prisons</td>
<td>Public dosing</td>
</tr>
<tr>
<td><strong>Private OTP clinics</strong></td>
<td></td>
</tr>
<tr>
<td>Community pharmacies</td>
<td>Private dosing</td>
</tr>
<tr>
<td><strong>Prescribers</strong></td>
<td></td>
</tr>
<tr>
<td>Public</td>
<td>Private</td>
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</tbody>
</table>

For more information about the administrative and legal framework of the Opioid Treatment Program see chapter 9, *Legal and administrative requirements* on page 91.
1.11.3 General practitioners

A number of general practitioners are authorised prescribers and provide opioid treatment as well as primary care medicine, sometimes undertaking the case management role for patients, or sharing this role with staff from the local drug and alcohol service.

1.11.4 Nurse practitioners

Amendments to the *NSW Poisons and Therapeutic Goods Regulations 2002*, gazetted in March 2006, allow for nurse practitioners to prescribe, possess, use and supply Schedule 8 drugs of addiction under approved guidelines. Drug and alcohol nurse practitioners may operate as opioid treatment prescribers in either public or private sectors, although it is foreseen that nurse practitioner prescribing will have a greater application in public health settings.

For the purposes of this document, the generic term “prescriber” should be considered to include drug and alcohol nurse practitioners.

1.11.5 Public hospitals

Dosing is provided in some public hospitals, especially in rural areas through local district hospitals. Public hospitals have the capacity to provide dosing for methadone, buprenorphine and other treatments through pharmacy departments, outpatients and (on a limited basis) emergency departments.

1.11.6 Prisons and juvenile detention centres

Methadone and buprenorphine treatment is provided in prisons and juvenile detention centres under the management of Justice Health. Patients who are taking methadone or buprenorphine when entering prison or detention will have this continued, subject to clinical review. Some individuals may commence treatment in prison. Patients who are taking methadone or buprenorphine when released are referred to community-based service providers to maintain continuity of care.

Further information


For enquiries regarding methadone or buprenorphine in prison the Justice Health Drug and Alcohol Liaison Officer can be contacted on (02) 9289 5948.

1.12 Social justice

The Opioid Treatment Program in NSW is founded upon social justice principles. Particular attention is directed to subgroups of illicit drug users with special needs and among whom health status reflects some disadvantage (such as Aboriginal and Torres Strait Islanders and people of non-English speaking backgrounds).

Further information

Drug and Alcohol Multicultural Education Centre (DAMEC)
DAMEC helps bridge service gaps by assisting alcohol and other drugs service providers improve access for non-English-speaking-background (NESB) clients.
DAMEC also works with NESB Communities to develop resources and information on alcohol and other drugs. <www.damec.org.au>

NSW Multicultural Health Communication Service (Multicultural Communication) provides information and services to assist health professionals to communicate with non-English-speaking communities throughout NSW. <www.mhcs.health.nsw.gov.au>
2 Clinical pharmacology

Chapter summary

- Opioid drugs (heroin, morphine, methadone and many others) produce their effects by acting on receptors (μ or OP3, κ or OP2, and δ or OP1, and OP4) at the molecular (cellular) level of the nervous system. Opioid compounds can be divided into pure agonists (eg, heroin, methadone), partial agonists (eg, buprenorphine), agonist–antagonists (eg, pentazocine) and antagonists (eg, naloxone).

- Repeated use of opioids produces tolerance, in which exposure to a drug results in the diminution of an effect or the need for a higher dose to maintain an effect; and physical dependence, in which the withdrawal of opioids produces unpleasant symptoms. Tolerance and physical dependence are also referred to as neuroadaptation to opioids.

- Signs and symptoms of opioid withdrawal include irritability, anxiety, restlessness, apprehension, muscular and abdominal pains, chills, nausea, diarrhoea, yawning, lacrimation, piloerection, sweating, sniffing, sneezing, rhinorrhea, general weakness and insomnia. Signs and symptoms usually begin 36–48 hours after last methadone dose, and 6–24 hours after last heroin dose.

- Methadone pharmacology:
  - onset of effects: 30 minutes
  - peak effects: about 3 hours
  - half-life: 14–58 hours
  - blood levels continue to rise during the first week of daily dosing
  - time to stabilise methadone levels in the body: 5–10 days
  - side effects: as for heroin
  - withdrawal onset: 36–48 hours, peak intensity within 5–7 days.

- Methadone drug interactions:
  - Combination of methadone and other sedative drugs (opioids, alcohol, benzodiazepines, tricyclic antidepressants, major tranquillisers and sedating antihistamines) can be fatal.
  - Effects of methadone are reversed or inhibited by naltrexone and naloxone.
  - People who are taking 40 mg or more of methadone each day are likely to experience withdrawal symptoms if given a dose of buprenorphine.
  - Methadone is metabolised by the cytochrome P450 3A4 enzyme system. Drugs which induce this system can accelerate the metabolism of methadone and precipitate withdrawal; inhibitors of cytochrome P450 can slow the metabolism of methadone and produce overdose.
  - Caution: drugs used in the treatment of HIV infection alter methadone pharmacokinetics.

- In advanced liver disease, doses of methadone or buprenorphine may need to be reduced significantly. Patients with severe respiratory disease must be monitored closely.

- Methadone does not cause damage to any of the major organs or systems of the body. The major hazard is the risk of overdose, particularly at the time of induction to treatment and when methadone is used in combination with sedative drugs. Slow onset of action and long half-life of methadone mean that toxic effects may become life-threatening many hours after ingestion. Clinical vigilance is most important in the first 14 days of treatment.
Buprenorphine pharmacology:
- onset of effects: 30–60 minutes
- peak effects: about 1–4 hours
- half-life: 20–72 hours (mean 36 hours)
- time to stabilise buprenorphine levels in the body: 7–10 days
- side effects: as for heroin
- withdrawal onset: 3–5 days, symptoms generally milder than withdrawal from other opioids.

Buprenorphine drug interactions:
- Combination of buprenorphine and sedative drugs (opioids, alcohol, benzodiazepines, tricyclic antidepressants, major tranquillisers and sedating antihistamines) can be dangerous.
- Buprenorphine has a higher affinity for opioid receptors than naltrexone or naloxone. Very high doses of naloxone (10–35 mg) are required to reverse an overdose of buprenorphine.
- Buprenorphine can produce withdrawal in people with high plasma levels of another opioid drug. Buprenorphine can interfere with the effectiveness of other opioids given for analgesia.
- Buprenorphine is metabolised by the cytochrome P450 3A4 enzyme system, but current evidence suggests that other medications that induce or inhibit this system have minimal impact on buprenorphine’s effects.

Buprenorphine is safer in overdose than pure opioid receptor agonists. Respiratory depression from buprenorphine overdose is less likely, but intravenous use of buprenorphine can be fatal.

Two formulations of buprenorphine are used for opioid replacement therapy:
- Subutex: sublingual tablets of buprenorphine (uncoated oval white tablets available in three dosage strengths: 0.4 mg, 2 mg and 8 mg)
- Suboxone: sublingual tablets of buprenorphine with naloxone (uncoated hexagonal orange tablets available in two dosage strengths: 2 mg buprenorphine with 0.5 mg naloxone, and 8 mg buprenorphine with 2 mg naloxone). The addition of naloxone is designed to discourage the diversion of buprenorphine to unintended uses. Naloxone is an opioid antagonist with low availability by the sublingual route, but high availability by the parenteral route. When taken sublingually, Suboxone is an effective opioid; when injected, the naloxone is predominantly effective in the first 20–30 minutes, inducing withdrawal (after which the buprenorphine effect becomes apparent).
2.1 Basic opioid pharmacology

The contemporary term “opioid” is used to designate drugs whose actions resemble morphine but whose chemical structure could be quite different from opiate analgesics. The term “opioid” is now used to describe all of the compounds that interact with stereospecific opioid receptors in the central and peripheral nervous systems. They include natural and synthetic compounds as well as endogenous peptides. For example, morphine is a naturally-occurring opioid; heroin is a semisynthetic opioid derived from opium; and methadone is a synthetic opioid. The principal effects of opioids are analgesia, sedation, respiratory depression and euphoria. Opioids have varying potency, bioavailability, speed of onset and duration of effect.

Opioids produce their effects by acting on receptors (µ or OP3, κ or OP2, and δ or OP3, and ORL1) at the molecular (cell) level of the nervous system. Opioid compounds can be classified in four groups: pure agonists, partial agonists, agonist–antagonists and antagonists.

A partial agonist is a drug that binds to a receptor but does not produce maximum stimulation. Because it occupies the receptor it can prevent a concurrently administered agonist with weaker receptor affinity from producing its full agonist effect. This is most likely to occur when it is administered to a patient receiving high doses of a pure agonist. Buprenorphine is a partial agonist. There is an upper limit to the effect of partial agonists, even with increasing doses.

The mixed agonist–antagonist drugs produce agonist effects at one receptor and antagonist effects at another. Pentazocine, butorphanol and nalbuphine are agonist–antagonists.

Antagonist drugs have no intrinsic pharmacological action but can block the action of an agonist. Naloxone and naltrexone are opioid receptor antagonists, which can reverse the effects of agonists such as morphine and methadone. Opioid antagonists with a high affinity for opioid receptors can dislodge opioid agonists from the receptor, precipitating withdrawal. They are often used therapeutically to reverse the effects of opioid overdose.

Repeated use of opioids produces tolerance, in which exposure to a drug results in the diminution of an effect or the need for a higher dose to maintain an effect; and physical dependence, in which the withdrawal of opioids produces unpleasant symptoms (see section 2.1.2, Opioid withdrawal, on page 11). Tolerance and physical dependence are also referred to as neuroadaptation to opioids.

2.1.1 Effects of opioids

<table>
<thead>
<tr>
<th>Chief actions</th>
<th>Other actions</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>■ analgesia</td>
<td>■ decreased blood pressure</td>
<td>■ sleep disturbances</td>
</tr>
<tr>
<td>■ sedation</td>
<td>■ constriction of the pupils</td>
<td>■ nausea and vomiting</td>
</tr>
<tr>
<td>■ respiratory depression</td>
<td>■ gastrointestinal tract actions:</td>
<td>■ constipation</td>
</tr>
<tr>
<td>■ euphoria (oral methadone causes less euphoria than intravenous heroin)</td>
<td>■ reduced gastric emptying</td>
<td>■ dry mouth</td>
</tr>
<tr>
<td></td>
<td>■ reduced motility</td>
<td>■ increased sweating</td>
</tr>
<tr>
<td></td>
<td>■ elevated pyloric sphincter tone</td>
<td>■ vasodilation and itching</td>
</tr>
<tr>
<td></td>
<td>■ elevated tone of sphincter of oddi can result in biliary spasm</td>
<td>■ menstrual irregularities in women</td>
</tr>
<tr>
<td></td>
<td>■ endocrine actions including:</td>
<td>■ gynaecomastia in men</td>
</tr>
<tr>
<td></td>
<td>■ reduced follicle stimulating hormone</td>
<td>■ sexual dysfunction, including impotence in men</td>
</tr>
<tr>
<td></td>
<td>■ reduced luteinising hormone</td>
<td>■ fluid retention and weight gain</td>
</tr>
<tr>
<td></td>
<td>■ elevated prolactin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>■ reduced adrenocorticotropic hormone</td>
<td></td>
</tr>
<tr>
<td></td>
<td>■ reduced testosterone (may return to normal after 2–10 months on methadone)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>■ elevated antidiuretic hormone</td>
<td></td>
</tr>
<tr>
<td></td>
<td>■ suppressed cough</td>
<td></td>
</tr>
</tbody>
</table>

Note: The effects listed here are effects of chronic opioid consumption, not specific to methadone or buprenorphine.
2.1.2 Opioid withdrawal

The signs and symptoms of opioid withdrawal include irritability, anxiety, restlessness, apprehension, muscular and abdominal pains, chills, nausea, diarrhoea, yawning, lacrimation, piloerection, sweating, sniffing, sneezing, rhinorrhea, general weakness and insomnia. Signs and symptoms usually begin 2–3 half-lives after the last opioid dose (i.e., after 36–48 hours for long half-life opioids such as methadone, and after 6–24 hours for short half-life opioids such as heroin and morphine).

Symptoms of withdrawal from heroin reach peak intensity within 2–4 days, and most of the obvious physical signs of withdrawal cannot be observed after 7 days.

| Assessment tools for measuring the severity of opioid withdrawal are available in Appendix A (page 100). |

Opioid withdrawal is rarely life-threatening. However, completing withdrawal is difficult for most people. The severity of withdrawal is influenced by the duration of opioid use, general physical health, and psychological factors, such as the reasons for undertaking withdrawal and fear of withdrawal.

2.2 Methadone

Methadone is a synthetic opioid agonist which is rapidly absorbed from the gastrointestinal tract, with measurable concentrations in plasma within 30 minutes of oral administration. Peak plasma concentrations after an oral dose are generally between 2 to 4 hours. Methadone is widely distributed throughout the body, with a volume of distribution of approximately 3–5 L/kg. It has a highly variable elimination half-life (14–58 hours). The effects of methadone are qualitatively similar to morphine and other pure agonist opioids. The clinical pharmacology of methadone makes it a very good agent for the treatment of opioid dependence.

The product information for Methadone Syrup is included in Appendix B (page 104).

<table>
<thead>
<tr>
<th>Methadone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Onset of effects:</strong> 30 minutes</td>
</tr>
<tr>
<td><strong>Peak effects:</strong> about 3 hours</td>
</tr>
<tr>
<td><strong>Half-life:</strong> 14–58 hours</td>
</tr>
<tr>
<td><strong>Blood levels continue to rise during the first week of daily dosing</strong></td>
</tr>
<tr>
<td><strong>Time to stabilise methadone levels in the body:</strong> 5–10 days</td>
</tr>
</tbody>
</table>

2.2.1 Side effects

Most people who have used heroin will experience few side effects from methadone. Methadone, like heroin, has effects on cognitive ability and attention. Symptoms of constipation, sexual dysfunction and (occasionally) increased sweating can persist for the duration of methadone treatment. The experience of side effects can reduce the compliance of the patient.

2.2.2 Pharmacology and pharmacokinetics

Methadone is fat soluble and binds to a range of body tissues including the lungs, kidneys, liver and spleen. The concentration of methadone in these organs is much higher than in blood. There is then a fairly slow transfer of methadone between these stores and the blood. Because of its good oral bioavailability (90%) and long elimination half-life, methadone is taken in an oral daily dose.

Methadone is primarily broken down in the liver via the cytochrome P450 enzyme system. About 10% of methadone administered orally is eliminated unchanged. The rest is metabolised and the (mainly inactive) metabolites are eliminated in the urine and faeces. Methadone is also secreted in sweat and saliva.

There is wide individual variability in the pharmacokinetics of methadone but in general, blood levels rise for about 2–4 hours after an oral dose and then begin to fall. Onset of effects occurs about 30 minutes after ingestion. The apparent half-life of the first dose is 12–18 hours, with a mean of 15 hours. With ongoing dosing, the half-life of methadone is extended to 13–47 hours, with a mean of 24 hours. This prolonged half-life contributes to the fact that methadone
blood levels continue to rise during the first week of daily dosing and fall relatively slowly between doses.

With daily dosing, methadone levels in the body reach a steady state (where drug elimination equals drug administration) after about 5–10 days. Thereafter variations in blood concentration levels are relatively small and good suppression of withdrawal is achieved. However, some patients may experience withdrawal symptoms before their next dose is due. If dose increases or split daily dosing do not prevent this, buprenorphine may be a better alternative.

2.2.3 Withdrawal

Symptoms of withdrawal from methadone usually begin 36–48 hours after the last dose and reach peak intensity within 5–7 days. Most of the obvious physical signs of withdrawal cannot be observed after 21 days, but a general feeling of reduced wellbeing and periodic strong cravings for opioids may continue for weeks or even months. Because withdrawal from methadone takes longer than withdrawal from heroin, untreated methadone withdrawal symptoms may be perceived as more unpleasant than those of heroin withdrawal.

2.2.4 Drug interactions

Toxicity and death have resulted from interactions between methadone and other drugs.

Other sedatives: The combination of methadone and other sedative drugs, including opioids, alcohol, benzodiazepines, tricyclic antidepressants, major tranquilisers and sedating antihistamines can be fatal.

Opioid antagonists: The effects of methadone are reversed or inhibited by naltrexone and naloxone.

Buprenorphine: People who are taking 40 mg or more of methadone each day are likely to experience withdrawal symptoms if given a dose of buprenorphine.

Transfer from high-dose methadone to buprenorphine is being trialed by a several centres, but at present it is recommended that patients receiving methadone not transfer to buprenorphine without first reducing their dose below 40 mg/day (see section 4.4.2.1, Transferring from methadone to buprenorphine, on page 31).

Opioid agonists: Taking other opioids while receiving methadone compounds the pharmacodynamic effects of methadone and may cause overdose and death.

Hepatic enzyme inhibitors and inducers: Methadone is metabolised by the cytochrome P450 3A4 enzyme system. Drugs which induce this system can accelerate the metabolism of methadone and precipitate withdrawal; inhibitors of cytochrome P450 can slow the metabolism of methadone and produce overdose. Specialist advice and caution are required if medications affecting cytochrome P450 are to be prescribed to patients receiving methadone.

Highly active antiretroviral therapy (HAART): Drugs used in the treatment of HIV infection alter methadone pharmacokinetics and caution must be exercised in patients receiving HAART.

A more detailed list of drugs that interact with methadone appears at Appendix D (page 111).

2.2.5 Concurrent medical illness and methadone/buprenorphine

Some patients receiving methadone or buprenorphine treatment have concomitant medical problems that may alter the pharmacokinetics of the drugs being prescribed. In those with advanced liver disease, doses of both methadone and buprenorphine may need to be reduced significantly. Progressive liver disease, such as may be seen in hepatitis C, may require gradual reduction of previously tolerated doses. In renal failure, dosage levels should also be monitored closely to ensure that dosing is safe.

In patients with severe respiratory disease, doses should be monitored closely to avoid significant respiratory depression and respiratory failure.
2.2.6 Safety

There are few long-term side effects of methadone taken orally in controlled doses. Methadone does not cause damage to any of the major organs or systems of the body and those side effects which do occur are considerably less harmful than the risks of alcohol, tobacco and illicit opioid use. In the long term patients may experience weight gain, sweating, poor sleep and dental problems. The major hazard associated with methadone is the risk of overdose. This risk is particularly high at induction to methadone treatment and when methadone is used in combination with sedative drugs. The relatively slow onset of action and long half-life mean that methadone overdose can be highly deceptive, with toxic effects that may become life-threatening many hours after ingestion. Because methadone levels rise with successive doses during induction into treatment, most deaths in this period have occurred on the third or fourth day. Clinical vigilance is most important in the first 14 days of treatment. Methadone is extremely toxic to non-tolerant individuals, especially children. All measures should be taken to ensure that parents understand the dangers of methadone and store any takeaway doses safely.

2.2.7 Formulations

Two preparations are available for methadone treatment in Australia:

- Methadone Syrup® from GlaxoSmithKline. This formulation contains 5 mg/mL methadone hydrochloride, sorbitol, glycerol, ethanol (4.75%), caramel, flavouring, and sodium benzoate (see product information in Appendix B on page 104).
- Biodone Forte® from McGaw Biomed. This formulation contains 5 mg/mL methadone hydrochloride and permicrol-red colouring (see product information in Appendix C on page 107).

2.3 Buprenorphine

Buprenorphine is a partial (μ receptor) opioid agonist derived from the morphine alkaloid, thebaine. The clinical pharmacology of buprenorphine makes it a good agent for opioid replacement therapy, and for the treatment of opioid withdrawal.

The product information for buprenorphine and buprenorphine–naloxone is included in Appendices E and F (page 114).

2.3.1 Effects

Buprenorphine has less euphoric and sedating effect than pure opioid agonists such as heroin, morphine and methadone. Nevertheless, its intrinsic activity is usually sufficient to diminish cravings for heroin and prevent or alleviate opioid withdrawal in people with opioid dependence. Buprenorphine has a strong affinity to opioid receptors, and can reduce the effect of heroin or morphine use by preventing these drugs from occupying the receptors.

2.3.2 Pharmacology and pharmacokinetics

Buprenorphine has poor oral bioavailability because it undergoes an extensive first pass metabolism in the small intestine and the liver. It has moderate (30%–40%) sublingual bioavailability, with the tablets taking between 2 and 7 minutes to dissolve. The speed of dissolution may be enhanced by breaking the tablets into a few pieces (this may also help reduce diversion of the dose). Crushing the tablets into powder should be avoided, as it tends to encourage swallowing.

Because buprenorphine is a partial agonist, its physiological and intoxicating effects usually plateau at a sublingual dose of 4–8 mg (some patients report greater intoxication with higher doses). For this reason, people who are used to high doses of heroin or methadone may find buprenorphine an unsatisfactory alternative.

For most patients, the maximal therapeutic effects of buprenorphine occur in the 12–24 mg dose range.
Buprenorphine has a higher affinity for opioid receptors than heroin or methadone and can displace these drugs from the opioid receptor, potentially precipitating opioid withdrawal in a person who has recently used methadone or heroin.

Buprenorphine is highly bound to plasma proteins. It is metabolised by the liver via the cytochrome P450 enzyme system (CYP 3A4) into norbuprenorphine and other metabolites, which are excreted in the faeces (70%) and urine (30%). The half-life of buprenorphine is highly variable: 20–72 hours, with a mean of 36 hours. With stable dosing, steady state levels are achieved over 7 days. Peak clinical effects occur 1–4 hours after sublingual administration, with continued effects for up to 12 hours at low doses (2 mg), but as long as 72 hours at higher doses (24–32 mg).

2.3.3 Withdrawal

The symptoms and signs of withdrawal from buprenorphine are similar to those found in withdrawal from other opioids, but withdrawal from buprenorphine is generally milder than withdrawal from methadone or heroin because of its slow dissociation from the μ receptor. Symptoms commence generally within 3–5 days of the last dose and can last for several weeks. Because buprenorphine is a partial agonist, its physiological and intoxicating effects usually plateau at a sublingual dose of 4–8 mg. For this reason people who are used to the sedating effects of methadone or heroin may find the clear headedness of buprenorphine unsatisfactory.

2.3.4 Drug interactions

Other sedatives: The combination of buprenorphine and sedative drugs, including opioids, alcohol, benzodiazepines, tricyclic antidepressants, and major tranquillisers and sedating antihistamines can be dangerous (deaths have been reported).

Opioid antagonists: Buprenorphine has a higher affinity for opioid receptors than naltrexone or naloxone. Very high doses of naloxone (10–35 mg) are required to reverse an overdose of buprenorphine.

Opioid agonists: Buprenorphine can produce withdrawal if taken by people while other opioids are active. For this reason, patients receiving methadone cannot easily transfer to buprenorphine without first reducing their dose below 40 mg/day (see section 4.4.2.1, Transferring from methadone to buprenorphine, on page 31). Buprenorphine can also interfere with the effectiveness of other opioids given for analgesia.

Hepatic enzyme inhibitors and inducers: Buprenorphine is metabolised by the cytochrome P450 3A4 enzyme system. Theoretically, drugs which inhibit or induce activity of this enzyme may affect buprenorphine levels. Many drugs alter the activity of this enzyme, particularly most anticonvulsants, which induce it. However, there are no clinical case reports of significant interactions with buprenorphine.

A more detailed list of drugs that interact with buprenorphine appears at Appendix G (page 127).

2.3.5 Safety

Because of the ceiling on its effect on respiratory depression and poor oral bioavailability, buprenorphine is safer in overdose than pure opioid receptor agonists. Respiratory depression from buprenorphine (or buprenorphine–naloxone) overdose is less likely than from other opioids. However, significant respiratory depression can occur if buprenorphine is administered intravenously.

There is no evidence of organ damage with chronic use of buprenorphine, although increases in liver enzymes are sometimes seen. There is no evidence of significant disruption of cognitive or psychomotor performance with buprenorphine maintenance dosing.

2.3.6 Formulations

Two formulations of buprenorphine are used for opioid replacement therapy:

Subutex (Reckitt Benckiser): sublingual tablets of buprenorphine (uncoated oval white tablets available in three dosage strengths: 0.4 mg, 2 mg and 8 mg).

Suboxone (Reckitt Benckiser): sublingual tablets of buprenorphine with naloxone (uncoated hexagonal orange tablets available in two dosage strengths: 2 mg buprenorphine with 0.5 mg naloxone, and 8 mg buprenorphine with 2 mg naloxone). The addition of naloxone is designed to discourage the diversion of buprenorphine to unintended uses. Naloxone is an opioid antagonist with low availability by the sublingual route, but high availability by the parenteral route. When taken sublingually, Suboxone is an effective opioid; when injected, the naloxone is predominantly effective, inducing withdrawal.

The chemical structure of naloxone

HCl. 2H2O

![The chemical structure of naloxone](image)
3 Entry into an opioid treatment program

Chapter summary

- Aims of the initial assessment:
  - establish an effective therapeutic relationship and begin harm reduction
  - determine the patient's suitability for the opioid treatment program
  - enable the patient to make an informed decision about treatment
  - provide advice and resources to facilitate harm reduction
  - meet legislative requirements for the opioid treatment program
  - document an initial treatment plan.

- Key features of the initial assessment:
  - opioid use (detailed history, periods of abstinence, overdoses, current use)
  - other drug use (alcohol and other drugs, prescribed medications)
  - health status
  - psychosocial status
  - risk behaviours, risk of deliberate self-harm or suicide
  - dependent children
  - past treatment
  - motivation for treatment
  - physical examination
  - investigations (if indicated: urine drug screening; HIV, hepatitis B, hepatitis C)
  - domestic violence screening.

- Opioid dependence is identified by:
  - history taking (typical day history will identify some features of opioid dependence)
  - physical examination (injecting sites, signs of opioid intoxication or withdrawal)
  - corroborative evidence from other sources
  - urine tests for opioids.

- Methadone or buprenorphine treatment is indicated for people who are neuroadapted to opioids. For some patients with a history of opioid dependence and a high risk of returning to opioid use, it is reasonable to offer methadone or buprenorphine maintenance even when neuroadaptation is not evident.

- Contraindications:
  - severe hepatic or respiratory insufficiency
  - known hypersensitivity to the proposed drug formulation
  - inability to give informed consent.

- Buprenorphine is not recommended in pregnancy and breastfeeding.

- Precautions:
  - patients with acute asthma, acute alcoholism, head injury and raised intracranial pressure, ulcerative colitis, biliary and renal tract spasm, and patients receiving monoamine oxidase inhibitors or within 14 days of stopping such treatment
  - polydrug use
  - psychiatric illness
  - chronic pain.
See section

- Relative merits of methadone and buprenorphine:
  - more clinical experience with methadone
  - buprenorphine is safer in overdose, may need to be taken less often.
  - buprenorphine takes longer to administer (must dissolve in the mouth)
  - buprenorphine can be more easily diverted to improper uses because it is in tablet form (the buprenorphine-naloxone combination may discourage diversion to injecting drug use).

- Patients should be allowed an informed choice.

- All eligible patients merit prompt admission to treatment, but this is especially important for:
  - pregnant women
  - people with HIV and their opioid using partners
  - hepatitis B carriers and their opioid using partners
  - people being released from correctional institutions
  - people on a diversion program from the criminal justice system.

- If a patient is aged 16 or 17 years, a second opinion must be obtained before authority to prescribe methadone or buprenorphine can be granted.

- Prescribing methadone or buprenorphine to patients under 16 years of age requires an exemption to the provisions of the Children and Young Persons (Care and Protection) Act 1998 (NSW).

- The patient’s informed consent is required before treatment begins. Informing the patient requires:
  - explanation of treatment options, aims, policies and expectations
  - warning not to drive or operate machinery during the first 10 days of treatment, 3–4 days after an increase in dose or when taking other drugs (eg, benzodiazepines, alcohol or other central nervous system depressants).
  - written information about treatment, including the NSW Health documents Methadone maintenance treatment — essential information and the Methadone overdose card
  - signing of NSW Health’s Treatment Agreement
  - documentation of an initial treatment plan.

- Asking the patient to sign a release of information form for Health Insurance Commission data can help prevent “doctor shopping”.

- Encourage all patients to be screened for HIV, hepatitis B and hepatitis C.
3.1 Assessing potential patients

The aims of the initial assessment are to:

- establish an effective therapeutic relationship (engage the patient)
- determine the patient’s suitability for methadone or buprenorphine treatment
- enable the patient to make an informed decision about treatment
- provide advice and resources to facilitate harm reduction
- meet the legislative requirements (eg, gaining authority to prescribe for the patient — see chapter 9, page 91)
- document an initial treatment plan.

The initial assessment is an exchange of information and involves:

- gathering the data needed for informed decisions
- collaborative decision-making with the patient about treatment
- establishing patient treatment goals
- starting the treatment process.

The assessment should not be seen as a series of barriers the patient must pass through to gain entry to a program.

The assessment may be conducted in a variety of settings and by practitioners of differing professional training. Nevertheless, if methadone or buprenorphine treatment is considered appropriate, a physical assessment by the prescriber is required. Key features of initial assessment are listed in section 3.4 (page 18).

A patient transferred from another opioid treatment clinic or program must always be newly assessed by the receiving prescriber.

An initial assessment will usually take 45–90 minutes. This may be undertaken over a series of appointments, as general practitioners sometimes do, or in one consultation. The initial assessment will result in an initial management plan, which can be implemented directly.

Assessment is an ongoing part of treatment, in which further information (eg, about previous treatment experiences, changing drug habits and life conditions) and corroborative data will be collected to inform more comprehensive treatment plans.

3.2 Building an effective therapeutic relationship

Patients seeking treatment for their opioid dependence present with a mixture of attitudes and emotions. Sometimes they are in crisis, feeling out of control, vulnerable and desperate. They are often suspicious of people in positions of authority and may be apprehensive about the response they will receive from the assessor. Often patients have a clear idea of what they want, but are ambivalent about entering treatment programs because of all they entail. They may feel that methadone or buprenorphine treatment is a last resort, so feelings of failure and inadequacy can be prominent.

The initial assessment is an important opportunity to begin building an effective therapeutic relationship with the patient. Take a non-judgemental, empathetic and respectful approach from the outset. Show a willingness to listen and clearly elucidate the patient’s needs. Encourage the patient to participate actively in treatment decisions, communicate clearly and allow time for the patient to gain an understanding of what assistance is being offered and the reasoning behind it. It should be explained to the patient how the increases and decreases of doses are decided upon, the benefits of regular attendance and the correct method of sublingual absorption of buprenorphine.

3.3 Commencing harm reduction

A key task of the assessment is to identify the patient’s actual or potential problems related to their opioid dependence. The objectives of an individual’s treatment program can then be agreed upon and prioritised.

Harm reduction begins during this assessment process. For example, the medical history and physical examination may reveal untreated current illnesses. The patient can then be given information and offered appropriate referral or appropriate investigation and treatment. Another example is identifying needle sharing when assessing risk behaviours. At the assessment, provide brief counselling about less risky practices and needle exchange services, and seek an agreement to deal more fully with these issues on follow-up appointments.

3.3.1 Contraception

Contraception is an important subject to discuss with women commencing treatment. Many women cease ovulation during periods of uncontrolled drug use and resume ovulation as they stabilise on the program. If this change is unexpected it can easily result in unplanned pregnancy. It is desirable for the health and welfare of mother and baby that pregnancies should be planned, or at least delayed until the mother is healthier and life less chaotic.
3.4 Key features of the initial assessment

Opioid use

- opioids used, quantity, frequency, route of administration, duration of current episode of use, time of last use and use in the last three days
- severity of dependence (use the criteria outlined in the *The diagnostic and statistical manual of mental disorders 4th edition* [DSM-IV] definition of dependence; see section 1.6.2 on page 4)
- age at first use, regular use and dependence
- timing and duration of periods of abstinence
- episodes of overdose.

Other drug use

- alcohol, illegal and prescribed drugs, current medications
- overdose through polydrug use
- driving intoxicated and impaired.

Health status

- diseases from drug use (bloodborne viruses, other)
- intercurrent health conditions (psychiatric, general, pregnancy and contraception).

Psychosocial status

- social position — employment, education, vocational skills, housing, financial status, family
- psychological status — mood, affect, cognition
- risk behaviours, risk of deliberate self-harm or suicide
- sex work/unsafe sex
- violent behaviour
- (for women:) routine screening for domestic violence (see Appendix H on page 128)
- criminal history (past and current charges and convictions, time spent in jail, past history of violence)
- dependent children (child risk assessment is mandatory; see section 7.14, *Child protection*, on page 76).

Past treatment

- where
- when
- periods of abstinence
- degrees of success and acceptance of treatment.

Selection of treatment

- motivation for treatment
- trigger for seeking treatment
- patient goals for treatment episode.

Physical examination

- clinical signs related to drug use (injecting sites, intoxication, withdrawal (see Appendix I on page 132)
- evidence of medical problems (eg, liver disease, valvular heart disease).

Investigations

- urine drug screening tests may be indicated if there are concerns about the accuracy of the drug history and diagnosis and may also be useful to confirm other drug use
- investigations for HIV and hepatitis B and C are indicated if there is a history or possibility of unsafe injecting practices.

A comprehensive assessment module for opioid treatment is given in Appendix J (page 134).

3.5 Identifying opioid dependence

Opioid dependence is identified by:

- history taking
- physical examination
- corroborative evidence from other sources
- urine tests for opioids.

3.5.1 History

The assessment should include a careful history that documents the extent and duration of drug use and its impacts upon the patient’s life. Use the criteria of DSM-IV to deter-
mine whether a patient’s history indicates opioid dependence (see section 1.6.2 on page 4).

Many of the criteria defining opioid dependence may be identified through a thorough history of a recent day’s activities and substance use.

### 3.5.1.1 The typical day history

- Explain that you need to understand the impact drug use has on their day-to-day activities.
- Ask what time they wake up and why? People may wake earlier than they would wish because of an alarm clock, other noise (traffic, baby), depression or withdrawals.
- Ask how they feel when they wake up. Those dependent on drugs often report feeling “sick” or unwell. If they report the latter, ask them to describe their symptoms of withdrawal. It may also be useful to ask those who do not wake because of withdrawal how long after waking they experience withdrawal or first opioid use.
- Ask where and when the first use takes place. Do they leave enough drugs at bedtime to have something to alleviate withdrawal in the morning or do they need to obtain drugs after waking? This may identify risky behaviours (eg, sex work, criminal activity) or other priorities such as child care or work commitments.
- Ask them how their days start. Do they shower? Do they have breakfast? (Lack of nutrition is common in this group.) How do they spend their day? Who do they see? Where do they go? This may identify high-risk behaviours (eg, sharing of injecting equipment) and reveal how much drug seeking and drug using behaviour have priority over other activities.
- Ask about their social networks.
- Ask about evening activities. What do they enjoy? Is it easy to get off to sleep? Do they crash out, do they lay awake, do they sleep straight through? Many drug users sleep badly and may chase sleep with a cocktail of depressant drugs, which represent increased risk to the person.
- Ask about their social networks.
- Ask about evening activities. What do they enjoy? Is it easy to get off to sleep? Do they crash out, do they lay awake, do they sleep straight through? Many drug users sleep badly and may chase sleep with a cocktail of depressant drugs, which represent increased risk to the person.
- The criteria of tolerance and continued use despite progress may be identified by asking about the onset and development of their drug use.

### 3.5.1.2 Overdose

Most opioid dependent people have experienced an overdose and many have witnessed it in others, with those who inject being far more likely to overdose than those who smoke. Accidental overdoses result from variable tolerance and general health, variable drug purity and polydrug use (especially alcohol or benzodiazepines). Opioid users recently released from prison and not in an opioid treatment program are particularly prone to accidental overdose. High levels of psychiatric comorbidity in opioid users mean that intentional overdose is also common.

An overdose may be frightening and should be taken as an opportunity to engage the patient in treatment. It is also important to identify the intent behind the overdose and consider scheduling the patient if the overdose was a deliberate attempt at self-harm.

### 3.5.2 Physical examination

Look for the presence of injecting sites, and signs of opioid intoxication or withdrawal.

#### Signs and symptoms of opioid withdrawal

- Dilation of pupils
- Anxiety
- Muscle and bone ache
- Muscle cramps
- Sleep disturbance
- Sweating
- Hot and cold flushes
- Piloerection
- Yawning
- Lacrimation
- Rhinorrhea
- Abdominal cramps
- Nausea
- Vomiting
- Diarrhoea
- Palpitations
- Rapid pulse
- Raised blood pressure

#### Signs of opioid intoxication

- Constriction of pupils
- Itching and scratching
- Sedation and somnolence
- Lowered blood pressure
- Slowed pulse
- Hypoventilation
- Pinpoint pupils
- Loss of consciousness
- Respiratory depression
- Hypotension
- Bradycardia
- Pulmonary oedema

### 3.5.3 Corroborative evidence

If possible, obtain corroborative evidence, such as a history of prior episodes of treatment for dependence, arrests for drug offences, and medical complications such as overdoses.

### 3.5.4 Urine tests

Test urine for the presence of opioids. A positive result is not definitive evidence of opioid dependence, but does provide a further piece of information about a patient’s opioid use. Methadone or buprenorphine treatment should not be delayed pending the result of urinalysis. If a negative result is returned after treatment begins, and the clinical picture is one of very low tolerance to opioids, reassess the patient’s level of opioid dependence.
3.6 Indications for methadone or buprenorphine treatment

Methadone or buprenorphine treatment is suitable only for individuals who are opioid dependent (see the DSM-IV definition in section 1.6.2 on page 4).

Opioid dependence is a complex condition, characterised by drug use becoming a central and dominant part of the person's life. It may or may not be accompanied by neuroadaptation (ie, opioid tolerance and withdrawal symptoms when without opioids). In general, people who are not neuroadapted are not suitable for maintenance treatment. However, in some circumstances it is reasonable to offer these treatments even when neuroadaptation is not evident. For example, some people with long histories of dependence may seek treatment after a period of abstinence when they feel there is a strong likelihood of relapsing into regular use. Others may have been opioid dependent, and become abstinent during a period in prison. After release, they realise that they are likely to relapse, and seek maintenance treatment.

If there is no current neuroadaptation to opioids (ie, no withdrawal symptoms on stopping use) initiation of methadone treatment must be cautious, with initial doses of no more than 20 mg/day for the first week. Buprenorphine may be a more suitable option for such patients.

If in doubt as to whether a person is suitable for maintenance treatment, it is highly desirable to seek a second opinion.

3.7 Specialist second opinion

The role of Area Drug and Alcohol Services is to provide a consultation-liaison service to primary care, mental health and general hospitals.

This involves the development of policies and procedures for health services, providing training to ensure their effective implementation, and consulting support to assist with complex cases. It may also involve joint management of some patients.

In relation to methadone and buprenorphine treatment, there are several circumstances in which prescribers should seek second opinions. Specifically, all prescribers should obtain a second opinion before implementing a treatment plan including:

- use of high dose methadone (200 mg or above)
- use of high dose buprenorphine (over 32 mg)
- treatment of people aged under 18 years.

In addition, practitioners are encouraged to seek review of complex cases (eg, pregnancy or cases presenting contentious issues) as part of maintaining good standards of care.

Many of these issues are addressed through applications to the Pharmacotherapy Credentialling Subcommittee. It is appropriate that the issues be dealt with by consultation, and Area Health Services should provide a prompt consultation service to support practitioners involved in opioid treatment.

It is the responsibility of Area Health Services to provide consulting services to address these issues, and these notes outline the approach Area Health Service specialists should adopt.

3.8 Contraindications to methadone or buprenorphine treatment

3.8.1 General contraindications

1 Severe hepatic or respiratory insufficiency.

2 Known hypersensitivity to the proposed drug formulation (naloxone allergy/sensitivity). Buprenorphine–naloxone should not be used in people with a known allergy to naloxone).

3 Inability to give informed consent: such as patients with major psychiatric illness or children under the age of 16 years. In the case of patients with psychiatric illness, the first priority is generally to control the mental disorder. If methadone or buprenorphine treatment seems to be required, seek a second opinion from a drug and alcohol medical specialist or drug and alcohol nurse practitioner and check the jurisdictional requirements regarding obtaining legal consent. In the case of children, see sections 3.11.2 and 3.11.3 (page 22).

3.8.2 Specific contraindications to buprenorphine

1 Pregnancy and breastfeeding. There are, as yet, insufficient data on the safety of buprenorphine in pregnancy and breastfeeding. Currently it is recommended that patients not commence treatment with buprenorphine if they are pregnant or breastfeeding, but those taking the drug when they conceive may choose to continue. See section 7.12.1 (page 74) for more detailed information on this subject.
2 Transfer from high-dose methadone maintenance. Patients who have been receiving more than 40 mg/day of methadone are likely to experience withdrawal if transferred to buprenorphine. See section 4.4.2.1 (page 31) for more information on transferring from methadone to buprenorphine.

3.9 Precautions

1 Medical conditions. Methadone and buprenorphine should be prescribed with caution for patients with acute alcohol dependence, head injury and raised intracranial pressure, ulcerative colitis, biliary and renal tract spasm, and for patients receiving monoamine oxidase inhibitors or within 14 days of stopping such treatment. Seek specialist advice in these cases.

For more on medical conditions with implications for treatment, see the product information for methadone (Appendices B and C, page 104) and buprenorphine (Appendices E and F, page 114).

2 Polydrug use. Treatment with methadone or buprenorphine should be approached cautiously in individuals using other drugs, particularly sedative drugs such as alcohol or benzodiazepines. Particular emphasis should be given to assessing the level of physical dependence on opioids, the likelihood of continued use of other sedative drugs, and the risk of overdose.

3 Psychiatric illness. Proceed with caution when assessing:
   • patients whose mental state impairs their capacity to provide informed consent
   • patients at risk of suicide or deliberate self-harm.

Patients with serious mental illness — particularly chronic schizophrenia, and those with unstable moods and a history of impulsive self-harm — probably require the structure and close monitoring afforded by supervised dosing.

If patients have a history of mental illness, but appear stable, it may be appropriate to seek a second opinion from another addiction specialist (psychiatrist) if considering the patient for unsupervised dosing.

4 Chronic pain. Patients with chronic pain require specialist management.

3.10 Relative merits of methadone and buprenorphine

Over 30 years of clinical experience and research has established that methadone in doses of 60–100 mg/day is highly effective at retaining people in treatment, suppressing heroin use and associated crime, and reducing the risk of overdose and bloodborne virus transmission. Recent trials have suggested that buprenorphine maintenance is also effective in achieving these objectives, although slightly less effective than methadone. However, some patients prefer buprenor-
3.11 Special patient groups

3.11.1 Priority patients

Entry into an opioid treatment program of a person suitable for treatment should not be delayed. If delays are unavoidable, people with certain conditions have priority, based upon the risk that non-treatment poses to the health of the wider community. These people are:

- pregnant women who are eligible for methadone maintenance treatment and their opioid using partners
- people with HIV and their opioid using partners
- hepatitis B carriers (HBsAg, HBeAg positive, or HBeAg negative but HBV DNA positive) and their opioid using partners
- people on a diversion program from the criminal justice system.

3.11.2 Patients aged 16–17 years

The second opinion in favour of treatment must be documented. In such instances, buprenorphine may be preferred over methadone due to its lower risk of harm in overdose and less severe withdrawal syndrome.

3.11.3 Patients aged under 16 years

The request for an exemption should include a second opinion from a drug and alcohol medical specialist nominated by the Area Health Service. To seek an exemption, the prescriber must apply in writing to the Director-General through the Chief Pharmacist located at the Pharmaceutical Services Branch. The request for exemption will be forwarded on behalf of the Director-General to the Department of Community Services.

Alternative dosing times may need to be considered for this special patient group.

3.12 Informed consent and the treatment plan

Patients’ informed consent is required before treatment begins.

For patients to make a fully informed decision, introduce and explain the following during the initial assessment:

- treatment options
- the nature of methadone or buprenorphine treatment (including the aims, what it can and cannot achieve, known benefits and drawbacks)
- the Treatment Agreement (see section 3.12.4 on page 24)
- the program policies and expectations (including the frequency of and procedures for dosing, urine testing, dosing hours, rules for takeaway doses, clinic or pharmacy schedule of appointments and rules regarding violence, drug dealing and drug use)
- the expected duration of treatment
- the side effects and risks associated with treatment
- details of when the patient would receive their first dose
- the potential effect on activities such as driving motor vehicles and operating machinery (see section 3.12.2 on page 23)
- the risks of other drug use (including alcohol) while taking methadone or buprenorphine
- that treatment, once commenced, should not be stopped suddenly
- that, if the patient has stabilised at three months, they may be expected to pick up their dose from a chemist, and that this will incur additional costs
- how to obtain further information (eg, NSW Alcohol and Drug Information Service [ADIS])
- a description of the Methadone Advice and Complaints Service (MACS).
3.12.1 Written information for the patient

Provide patients who are assessed as suitable for methadone or buprenorphine treatment with written information about all aspects of the treatment program being offered, their rights and responsibilities, and the conditions under which they might be involuntarily discharged from the program. Staff should be aware of patients with literary difficulties and assess their understanding of the key documents.

An example of a patient information form is given in Appendix K (page 145).

All patients should receive the following documents:

- the NSW Health Methadone overdose card and patient information booklet, Methadone maintenance treatment — essential information, or the patient information booklet for buprenorphine or buprenorphine–naloxone produced by the drug manufacturer, Reckitt Benckiser.
- the NSW Health leaflet Your Kid’s Safety — advice for parents on storing methadone, safe sleeping and settling.

3.12.2 Special warning: fitness to drive

Methadone or buprenorphine treatment may affect the capacity of patients to drive or operate machinery, particularly:

- during the first 7–10 days of commencing treatment
- 3–4 days after an increase in dose
- when they also take other drugs (eg, benzodiazepines, alcohol or other central nervous system depressants).

Patients must be warned about these effects before they enter treatment, when the dose of methadone or buprenorphine is increased, or when it appears that they may be using other drugs. To ensure that clinicians have fulfilled their responsibilities, the advice given should be clearly documented in the patient notes. It is recommended that patients receive an information card regarding fitness to drive while in opioid treatment.

Until patients are stabilised on a particular dose of methadone or buprenorphine, it is safer if they avoid driving a car or operating machinery. Once stabilised and with unchanging doses, it is unlikely that driving skills will be impaired unless other drugs are consumed.

Primary responsibility to assess fitness to drive and to inform patients of the potential risk rests with the prescriber, but other health professionals involved in dosing and case management are also responsible for advising patients not to drive if there is any doubt about their fitness to do so at that time.

If a patient is determined to be unfit to drive, the prescriber must so advise the patient, tell him or her of the need to notify the Driver Licensing Authority and, if necessary, undertake processes required for a conditional license.

Under the Road Transport (Driver Licensing) Regulation, 1999 30 (5), “The holder of a driver licence must, as soon as practicable, notify the Authority of any permanent or long-term injury or illness that may impair his or her ability to drive safely.”

In addition to penalties under the legislation, patients may be liable at common law if they continue to drive knowing that they have a condition likely to adversely affect driving. Failure to report may also breach the terms of insurance.

There may be circumstances, such as a patient’s failure to report, under which a medical professional is required to report a patient’s unfitness to drive to the Driver Licensing Authority if there is a known impairment and a subsequent risk to road safety.

3.12.3 Documenting the initial treatment plan

At the assessment, the initial treatment plan should be developed in collaboration with the patient and documented. The initial treatment plan should document the decision on the choice of therapy. If the decision is not to prescribe methadone or buprenorphine, alternative management recommendations should be explained. If methadone or buprenorphine will be prescribed, the plan should justify the decision and the choice of opioid to be prescribed, and document:

- starting date and dose
- early monitoring arrangements
- initial harm reduction actions
- coordinated care and adjunct/ancillary services arrangements.

Further information

Further information
3.12.4 Treatment Agreement

All patients entering an opioid treatment program must sign a NSW Health Treatment Agreement before commencing treatment (Appendix M, page 163). The Agreement was developed to specify the rights and responsibilities of patients and clinicians involved in methadone or buprenorphine treatment. It outlines responsibilities regarding drug use, behaviour, appointments and service rules, takeaway doses, urine testing and treatment plans.

3.12.5 Coordinating care and shared care

Managing opioid dependence is a multidisciplinary task. Supporting a patient will often involve coordination between the prescriber, case manager, drug dispenser and other health professionals (particularly community pharmacists and general practitioners).

Ongoing communication between the prescriber of methadone or buprenorphine treatment, the drug dispenser and other professionals involved in managing the patient is essential to provide a safe environment for treatment and to ensure that regular feedback and monitoring from diverse health carers is available. This communication can be facilitated by the development of coordinated care plans.

3.12.6 Release of information forms

Under the Health Records and Information Privacy Act 2002 (NSW), information recorded in patient case notes, government forms or computer databases is confidential. The patient’s permission is required before any information is released to a person or agency not involved in the current episode of the patient’s treatment. This includes family or friends as well as organisations such as the Police or Social Agencies.

Some people exploit this confidentiality to go “doctor shopping”, seeking drugs from as many different providers as they can. Asking patients to sign a release of information agreement may prevent this practice.

The Health Insurance Commission (HIC) has a privacy release voluntary agreement form that authorises the HIC to provide relevant Pharmaceutical Benefit Scheme (PBS) prescribing information about a particular patient to a nominated practitioner. The nominated practitioner can use this authorisation to check what prescriptions the patient already has before writing any more.

The HIC also provides a Prescription Shopping Information Service, which can be used by any prescriber registered with the service to obtain information on the amount and type of PBS medicine recently supplied to any patient who might be seeking drugs in excess of medical need.

3.13 HIV, hepatitis B and hepatitis C screening

NSW Health will expect all drug and alcohol services to take responsibility for discussing bloodborne viruses and the risk of infection with their patients. New guidelines will be prepared, but until that time:

- Either at the assessment interview or after treatment has commenced, offer all patients screening for HIV, hepatitis B and hepatitis C and advise on the availability of hepatitis B vaccination.

- Tests should only be undertaken when patients have voluntarily agreed to such testing.

- To assist patients to make a decision regarding testing, provide sufficient information to allow them to give informed consent, and assure them that confidentiality will be maintained.

- If patients elect to undergo these tests, pre-test and post-test counselling must be provided as outlined in NSW Health Policy Directive PD2005_048: Counselling associated with HIV antibody testing — guidelines.

Encourage hepatitis A and hepatitis B vaccination for all patients except those who report recent completed vaccination. The Medicare Benefits Schedule does not cover vaccination, so cost may be an issue for some patients.

Further information


4 Commencing treatment

Chapter summary

- Patients need to begin methadone or buprenorphine treatment in a well supervised setting to ensure frequent monitoring. Special caution in relation to overdose is required with patients who have:
  - reduced or uncertain opioid tolerance
  - polydrug use, particularly central nervous system sedative use
  - concurrent alcohol dependence
  - psychiatric illness and/or psychiatric drug treatment
  - concomitant medical problems.

- Safety is improved by:
  - establishing a therapeutic relationship that fosters good communication between patient and prescriber
  - cautious initial dosing
  - repeated observation of the patient during the first week
  - careful explanation of intoxicating effects and withdrawal during the induction and maintenance phases of treatment.

- The treatment plan outlined at the initial assessment is developed during the first week of treatment in collaboration between the patient, the prescriber and other members of the treatment team. The plan should be reviewed at least every three months.

- When deciding on the starting dose, consider:
  - severity of dependence and level of tolerance (drug-use history, corroborative evidence, findings on examination and observation, urine testing, consultation with clinicians with previous experience of the patient).
  - time since last opioid use.
  - concomitant use of benzodiazepines or alcohol.
  - where dosing is to occur.

- If possible, patients should be observed for 3–4 hours after the first dose (ie, at the time of peak effect for methadone) for signs of toxicity or withdrawal.

- Starting dose, methadone. Caution: deaths in the first two weeks have been associated with methadone doses in the range 25–100 mg/day. A dose of 20 mg for a 70 kg patient can be presumed to be safe.

- The first dose of buprenorphine should not be given until at least 8–12 hours after the patient's last dose of heroin and at least 24–36 hours after the last dose of methadone. The patient should be in mild withdrawal. An 8 mg starting dose of buprenorphine will be tolerated by most patients and will lead to most rapid stabilisation. A dose of 16 mg should be aimed for by Day 3.

- Some patients may select slow increases in dose (perhaps fearing increased dependence or side effects), but this may result in continuing withdrawal symptoms and low retention in treatment.

- Higher dose induction schedule (eg, 8–16–24 mg) may be associated with toxicity or side effects (sedation, dizziness, nausea, headache), which can be treated by reducing the dose.

- Dose should not exceed 32 mg at the end of the first week (usually 24 mg or less).

- Transferring between treatments:
  - Appropriate methadone dose before transferring to buprenorphine is less than 40 mg/day. Patients should have been on this methadone dose for at least one week before commencing buprenorphine, and the last methadone dose should be at least 24 hours before the first buprenorphine dose.
  - Appropriate buprenorphine dose before transferring to methadone is less than 16 mg/day. The first dose of methadone can be taken 24 hours after the last dose of buprenorphine and should not exceed 40 mg. Patients transferring from lower doses of buprenorphine should receive lower doses of methadone.
  - Patients taking naltrexone rapidly lose tolerance to opioids. Patients transferring from naltrexone to opioid treatment should not receive methadone or buprenorphine until at least 72 hours after the last dose of naltrexone. Starting doses should be no greater than 20 mg of methadone or 4 mg of buprenorphine.
■ Stabilisation is about titrating the dose against the needs of the individual patient. Dose changes should only be made after the patient is assessed by the prescriber. Assessment should include:
  ◆ features of intoxication or withdrawal over the preceding 24 hours (patient’s self-report, examination)
  ◆ patient’s perception of dose adequacy and satisfaction with treatment
  ◆ patient’s adherence to dosing regimen
  ◆ other drug use (patient’s self-report, urine testing)
  ◆ side effects and adverse events (including intoxicated presentations and overdoses).

4.5 Titrating methadone dose:
  ◆ Decrease dose if there are features of intoxication 3–4 hours after dosing or if there are severe or intolerable side effects.
  ◆ Do not increase dose for at least the first 3 days of treatment unless there are clear signs of withdrawal 3–4 hours after dose.
  ◆ Consider dose increments of 5–10 mg every 3 days, subject to assessment. Total weekly increase should not exceed 20 mg.
  ◆ Maximum dose at the end of the first week should typically be no more than 40 mg.
  ◆ Warn patients not to drive or operate machinery during periods of dose adjustments.

4.5.2.2 Titrating buprenorphine dose:
  ◆ Buprenorphine doses can be increased rapidly with safety.
  ◆ Decrease the dose if there are features of intoxication at the time of peak effects (1–4 hours after dosing), or if there are severe or intolerable side effects.
  ◆ From Day 2 onwards, dose increases can be as much as 8 mg per day.
  ◆ The maximum daily dose at the end of the first week should be no more than 32 mg. The dose may be safely increased by 2–8 mg daily.
  ◆ There is rarely a reason to prescribe more than 32 mg/day of buprenorphine to any patient.
  ◆ To prescribe a dose in excess of 32 mg a day, approval must be sought through the Pharmacotherapy Credentialling Subcommittee.

4.5.3.2 Dose adjustment is an ongoing part of treatment. Maximum weekly increases:
  ◆ Methadone: 10 mg for patients receiving 40–100 mg/day, or 15 mg for patients receiving more than 100 mg/day.
  ◆ Buprenorphine: 8–24 mg.

4.6 Assessing patients’ drug use is essential for safe prescribing and dosing, a useful guide to progress in treatment and an aid to clinical decision-making. Drug monitoring does not work as well for these purposes if it is used as a basis for punitive actions against patients who continue to use illicit drugs. The available means of monitoring drug use are the patient’s self-report, urine testing and clinical observation. None are sufficient on their own. Liver function tests can be used to help assess alcohol abuse, which lessens the safety of methadone or buprenorphine treatment.

4.7 Legal requirements for starting methadone or buprenorphine treatment:
  ◆ Documented proof of identity of the patient.
  ◆ Authority to prescribe methadone or buprenorphine to the patient from the Pharmaceutical Services Branch of NSW Health. Authority is sought for each patient by completing a yellow Application for authority to prescribe methadone form, or a lilac Application for authority to prescribe buprenorphine form.
  ◆ A current photograph and/or a detailed written description, as well as a valid prescription, must be forwarded to the clinic or pharmacy where dosing will take place. Do not send the prescription or duplicates of the original to the dosing point with the patient.

4.8 All patients should commence treatment with methadone or buprenorphine in a well supervised setting. This will usually be a specialist clinic, but can also be community or hospital pharmacies, community or mental health centres and accredited general practitioner/prescriber surgeries.

■ The Pharmaceutical Services Branch of NSW Health must be notified of the dosing location.

■ Once stabilised in treatment, most patients should be dosed at retail pharmacies. Normally it takes about three months from starting methadone treatment and one to three months from starting buprenorphine treatment to adequately assess the patient’s suitability for pharmacy dosing. The pharmacist and prescriber or patient’s caseworker should communicate regularly (at least every three months), and dosing arrangements should be reviewed at least every six months.
4.1 Induction to an opioid treatment program

Patients need to begin opioid treatment in a well supervised setting to ensure frequent monitoring. Usually this will be a clinic in the public or private sector, but may be in a hospital ward or in a general practitioner’s rooms (section 4.8.2 on page 37 discusses suitability for pharmacy dosing).

Special caution is required with patients who have:

- reduced or uncertain opioid tolerance (e.g., recently released prisoners, or patients who have attempted abstinence)
- polydrug use
- concurrent alcohol dependence
- psychiatric illness and/or psychiatric drug treatment
- concomitant medical problems
- respiratory problems.

All new patients need to be made aware of state and local guidelines for treatment. Management problems can arise if these are not clearly explained at the outset.

The chief objectives during induction are to:

- retain the patient in treatment by minimising the discomfort of withdrawal
- ensure the patient’s safety.

Induction into treatment involves two processes:

1. Stabilisation (abolishing fluctuations between intoxication and withdrawal).
2. Developing tolerance (reducing the response to additional opioids).

Both processes decrease the patient’s need to use heroin.

4.1.1 Induction to methadone maintenance

Methadone can be fatal. Safety during induction is achieved by:

- establishing a therapeutic relationship that fosters good communication between patient and prescriber
- cautious initial dosing
- repeated daily observation of the patient during the first weeks of treatment
- careful explanation of intoxicating effects and withdrawal during the induction and maintenance phases of treatment and the risks of taking central nervous system depressants.

Generally speaking, withdrawal from illicit opioids will have begun before treatment commences. Safety requires that the initial dose of methadone is likely to be lower than needed for full control of the patient’s withdrawal symptoms. Methadone takes several days’ dosing to achieve its full clinical effect. It is particularly important to explain clearly that induction into maintenance treatment takes time, and that patients will experience increasing effects from treatment over the first few days even if the dose is not increased.

The prescriber must strike the right balance between relieving withdrawal symptoms and avoiding the risks of toxicity and sedation. Doses that are too high can be fatal, but inadequate doses may cause patients experiencing withdrawal symptoms to “top up” the prescribed dose with heroin, benzodiazepines or other drugs. This too can have lethal consequences.

Deaths during the induction phase of methadone treatment have been related to:

- concomitant use of other drugs (particularly sedatives such as alcohol and benzodiazepines)
- commencement on doses that are too high for the level of tolerance
- lack of understanding of the cumulative effect of methadone
- inadequate observation and supervision of dosing
- individual variation in the metabolism and tolerance of methadone, which is not possible to predict at assessment.

4.1.2 Induction to buprenorphine maintenance

There is less risk of death during induction to buprenorphine treatment, but caution is still essential, particularly if there is any possibility of the patient using other drugs with a sedative effect (e.g., alcohol, benzodiazepines). Nonetheless, it is usually safe to achieve rapid induction onto an effective maintenance dose of buprenorphine.
4.1.4 Equivalence of buprenorphine and buprenorphine–naloxone

Studies to date indicate that buprenorphine (Subutex) and buprenorphine–naloxone (Suboxone) are equally effective treatments. The addition of naloxone does not attenuate the opioid-agonist effects of buprenorphine. There are two important contraindications to buprenorphine-naloxone:

- Buprenorphine is not recommended for use in pregnancy or breastfeeding, but if it is being used because the patient wishes to continue an existing treatment regimen, the buprenorphine–naloxone combination should be avoided in favour of buprenorphine alone.
- Patients transferring from methadone to buprenorphine should be stabilised on buprenorphine alone before transfer to buprenorphine–naloxone.

The buprenorphine–naloxone combination may be less desirable as an injectable preparation in opioid dependent populations because its use can precipitate withdrawal in someone already affected by opioids. This may discourage diversion and subsequent intravenous use. However, the withdrawal effect is only temporary, and will be succeeded by opioid effects as the naloxone is eliminated and the long-term action of buprenorphine becomes dominant. Moreover, the naloxone has no effect if the dose is taken sublingually, or if the person is opioid-naïve or already in withdrawal.

For these reasons, buprenorphine–naloxone cannot be seen as the solution to problems with dose diversion, which must be managed by careful monitoring of dosing and the patient’s progress in treatment. Buprenorphine–naloxone may have advantages over buprenorphine alone in situations where monitoring of dosing may be less strict than in a specialist clinic (eg, pharmacy dosing) or for takeaway doses.
4.2 Induction to treatment flowchart

Initial assessment:
- Opioid use (detailed history, periods of abstinence, overdoses, current use)
- Other drug use (alcohol and other drugs, prescribed medications)
- Health status
- Psychosocial status
- Risk behaviours
- Domestic violence screening
- Contraception
- Dependent children (child risk assessment)
- Past treatment
- Motivation for treatment
- Physical examination
- Investigations (if indicated: urine drug screening; HIV, hepatitis B, hepatitis C)

Does patient meet criteria for opioid treatment program? Confirm:
- opioid dependence
- current level of neuroadaptation

NO
Consider alternatives

YES
Select drug and starting dose

Confirm patient identity (documentary proof required).

Informed consent required:
- explanation of treatment options and patient rights and responsibilities
- warning not to drive or operate machinery during first 10 days of treatment
- written information, including Methadone maintenance treatment — essential information and the Methadone overdose card
- signing of NSW Health’s Treatment Agreement
- documentation of an initial treatment plan.

Ask patient to sign a release of information form (to facilitate shared care)

If patient has a general practitioner and agrees to contact, inform general practitioner about the patient’s opioid treatment

Obtain authority to prescribe by lodging appropriate Application for authority to prescribe form with the Pharmaceutical Services Branch, and notify the Branch of the dosing point for the patient.

Obtain photos of patient (required for patient record and to accompany prescriptions)

First two weeks of treatment:
- monitor closely
- develop comprehensive treatment plan
- titrate dose to achieve stabilisation

Treatment plan: section 4.3
Stabilisation: section 4.5
Monitoring: section 4.6
4.3 Treatment plan

An initial treatment plan is developed at the first assessment (see section 3.12.3 on page 23). During the first week of treatment, this should be developed into a comprehensive treatment plan.

The treatment plan is developed in collaboration between the patient, the prescriber and other members of the treatment team (e.g., the case manager, the pharmacist or dispensing staff). It sets out the services to be provided and their timing. Elements of the plan include:

- dose review and adjustments
- setting and reviewing treatment goals
- medical and psychiatric review and treatments
- monitoring of progress
- harm reduction interventions (e.g., advice on reducing risks of contracting or spreading hepatitis and HIV infection)
- counselling
- assessment of suitability for retail pharmacy dosing and assistance in transfer of dosing to a pharmacy if suitable
- assistance with accommodation if required
- assistance with any vocational difficulties (e.g., linking into training or employment services)
- monitoring of parenting, particularly of children under 16 and linking into relevant services to assist parenting skill development
- assessment of suitability for gradual withdrawal from treatment
- assistance in reducing concurrent drug use.

Review the comprehensive treatment plan with the patient every three months. Note completed activities and progress towards goals. Before review with the patient, all members of the treatment team should contribute information and opinions to the review. An outcome of the review should be the development and documentation of a revised treatment plan for the next three months.

4.4 Starting dose

The first dose of methadone or buprenorphine should be determined for each patient based on the severity of dependence and level of tolerance to opioids.

The information gathered in the initial assessment (drug-use history, corroborative evidence, findings on examination, and urine testing) give an indication of a patient’s opioid tolerance, but do not define it with certainty.

A period of observation for signs and symptoms of opioid toxicity or withdrawal is a more accurate method of assessing opioid tolerance than history alone. If there is doubt about the degree of tolerance, a review of the patient when withdrawal symptoms are being experienced may help to resolve uncertainty about a safe starting dose.

Prescribers should make every effort to communicate with other clinicians who may have seen the patient previously to corroborate significant elements of the patient’s history and to assist in decisions about commencing treatment.

When deciding on the commencing dose, also consider:

- Where dosing is to occur (see section 4.8 on page 37).
  - Are staff and facilities available for observing and assessing the patient before and after dosing?
  - Who will assess the patient’s degree of withdrawal or intoxication before dosing? (Appendix I on page 132 lists intoxication and withdrawal states from commonly used drugs)
- Time since last opioid use and other drug or alcohol use.
  - The risk of overdose increases most markedly when other central nervous system depressants are also used.
- Concomitant use of benzodiazepines or alcohol (see also section 7.3, Managing polydrug use, on page 64).
  - If the patient shows signs of intoxication with benzodiazepines or alcohol, the dose should be withheld or reduced.

If at all possible, patients should be observed 3–4 hours after the first dose (i.e., at the time of peak effect) for signs of toxicity or withdrawal.

4.4.1 Starting dose for new treatment

Patients should be requested to present in mild observable withdrawal for their first dose and to refrain from other drugs (e.g., benzodiazepines or alcohol) since these mask symptoms of withdrawal or interact negatively with methadone and buprenorphine.

It should be explained to patients why it is necessary for them to be observed in mild withdrawal.

The aim of induction is to transfer the patient as quickly as possible onto the dose of buprenorphine or methadone that diminishes the discomfort of withdrawal and reduces the craving for other opioid drugs, without inducing significant toxicity or side effects.

4.4.1.1 Starting dose of methadone — start low and go slow

New patients should be dosed with caution. Deaths in the first two weeks have been associated with methadone doses in the range 25–100 mg/day, with most occurring at doses of 40–60 mg/day.
A dose of 20 mg for a 70 kg patient can be presumed to be safe, even in opioid-naïve individuals, as this is the lowest dose at which toxicity has been observed.

If the patient is experiencing persistent withdrawal symptoms at 4 hours, a supplementary dose of 5–10 mg can be considered.

Caution should be exercised for starting doses of 30 mg or more.

Extreme caution should be exercised if an initial dose of methadone exceeding 40 mg is considered necessary. Specialist consultation may be desirable, or inpatient admission to allow supervised induction of treatment.

### 4.4.1.2 Starting dose of buprenorphine

As buprenorphine will displace other opioids from opioid receptors but has less intrinsic opioid activity, it can precipitate withdrawal symptoms if given while other opioids are active. The first dose of buprenorphine (usually 4 mg) should not be given until at least 8–12 hours after the patient’s last dose of heroin and at least 24–36 hours after the last dose of methadone.

Treatment should not be commenced until the patient has a Clinical Opioid Withdrawal Scale (COWS) score of at least 8 (representing the mid point of the COWS scale) or 16–25 on the Subjective Opiate Withdrawal Scale (SOWS), representing mild to more moderate withdrawal.

Rapid higher dose induction (up to 16 mg by Day 3) with buprenorphine is both safe and effective, and is recommended to increase therapeutic effect and retention in treatment.

These measures are only a guide and should neither dictate management nor supersedes individual clinical assessment.

Patients who have been using heroin or other short-acting opioids can be equivalently inducted into treatment with either buprenorphine (Subutex) or buprenorphine–naloxone (Suboxone). Buprenorphine–naloxone may be preferable in situations where there may be less supervision of consumption and a greater risk of diversion, such as community pharmacies. Prescriptions may be written with either a fixed increasing dosage regimen (stipulating a certain dose on each of the induction days) or with a flexible schedule that allows the patient to remain on a given dose rather than increasing on a particular day. Variable schedules for doses should only be used where the prescriber can review the patient daily. Slow induction regimens may lead to suboptimal doses and decreased retention in treatment. A dose of 16 mg by Day 3 should be the goal for most patients, followed by clinical review and dose adjustment.

Patients should be advised that, because of buprenorphine’s competitive affinity for opioid receptors, continuing to use other opioids once they have started to take buprenorphine is unlikely to reduce their withdrawal symptoms.

### Buprenorphine induction regimen

- An 8 mg start will be tolerated by most patients and will lead to most rapid stabilisation.
- Encourage rapid induction (8–12–16 mg) and review patients daily
- Some patients may select slow increases in dose (perhaps fearing increased dependence or side effects), but this may result in low retention in treatment.
- Rapid induction (8–12–16 mg) may cause side effects (sedation, dizziness, nausea, agitation, headache), which can be treated by reducing the dose.
- Dose should not exceed 32 mg at the end of the first week (usually 16 mg or less).

### 4.4.2 Starting dose when transferring from another treatment

#### 4.4.2.1 Transferring from methadone to buprenorphine

A transfer from methadone to buprenorphine may be appropriate when:

- side effects of methadone are intolerable
- the patient wishes to change, perhaps in anticipation of withdrawing from treatment via dose reductions
- the patient has failed to achieve stability on methadone, showing erratic attendance for treatment or continued problematic drug use
- there are concerns over polydrug use.

In methadone patients, a dose of buprenorphine displaces methadone from opioid receptors, but has less agonist effect. Patients on low doses of methadone (30 mg/day or less) generally tolerate this transition with minimal discomfort. However, patients on higher doses of methadone may experience precipitated withdrawal.

The appropriate methadone dose before transferring to buprenorphine is less than 40 mg/day, and preferably less than 30 mg/day. Patients should have been on this methadone dose for at least one week before commencing buprenorphine.

Patients should not be transferred from methadone to buprenorphine–naloxone because of the risk of precipitated withdrawal (transfer to buprenorphine first, then to buprenorphine–naloxone after stabilising the dose).
The first dose of buprenorphine should be given at least 24 hours after the last dose of methadone. The first dose is usually 4 mg: lower doses are generally an inadequate substitute for methadone and higher doses increase the risk of precipitating withdrawal. The first dose is best given early in the day to permit the management of any significant transitional symptoms (eg, precipitated withdrawal).

Patients should be fully informed about the potential transitional effects, and reminded that use of heroin, codeine or other opioid drugs will complicate the transition. Make a contingency plan for dealing with severe transitional symptoms. Clonidine (100 μg every 3–4 hours) may be a useful medication for symptomatic relief.

For a patient transferring from 30 mg/day methadone or less:
- Delay the first dose of buprenorphine until the patient shows significant features of withdrawal. This is usually more than 24 hours after the last dose of methadone.
- Give 4 mg of buprenorphine as the first dose. Review the patient 3–4 hours after the first dose. If the patient is experiencing no increase in withdrawal severity and is still reporting withdrawal, give another 2–4 mg of buprenorphine.
- Review the patient again on Day 2, when the dose can generally be increased by up to 8 mg.

For a patient transferring from 40–60 mg/day of methadone:
- Delay the first dose of buprenorphine until the patient shows significant features of withdrawal. This is usually 48–96 hours after the last dose of methadone.
- Give 4 mg of buprenorphine as the first dose. Review the patient 3–4 hours after the first dose. If the patient is experiencing no increase in withdrawal severity, give another 2–4 mg of buprenorphine. If the patient is experiencing worsening withdrawal, give no further dose that day. Medications for symptomatic relief may be required (eg, clonidine 100 μg every 3–4 hours).
- Review the patient again on Day 2, when the dose can generally be increased safely by 8 mg.
- Subsequent doses can be increased freely.

Patients on higher doses of methadone who are unable to reduce their dose to 60 mg/day or less should not usually attempt transferring to buprenorphine. If such a transfer is required, it should only be attempted in a specialist clinic or with specialist support. If the patient is on a methadone dose above 40 mg then a specialist option should be sought.

Precipitated withdrawal can be severe when buprenorphine is taken after recently consumed methadone and should be managed aggressively if necessary. In most cases any withdrawal will be mild and short lived (4–8 hours after a 4 mg dose). Treatment may include clonidine, intramuscular nonsteroidal anti-inflammatory drugs and antiemetics. Supervision should be provided during the initial management of precipitated withdrawal and in some cases a brief admission may be required. The patient should wait at least another 24 hours before attempting buprenorphine dosing again.

### 4.4.2.2 Transferring from methadone to buprenorphine–naloxone

People who have been on long-term stable methadone treatment may seek to transfer to buprenorphine in order to eventually receive unsupervised dosing with buprenorphine–naloxone. Such patients should be strongly advised that there is a small but definite risk of their being destabilised by transferring from a drug on which they are being successfully treated. They should be cautioned against poorly informed decisions regarding this. Patients who were previously stable on methadone may be eligible to receive takeaway doses of buprenorphine–naloxone with further progression to unsupervised dosing, but only after demonstrating at least a month of maintained stability on buprenorphine.

Normally, transfer from methadone to buprenorphine is recommended when the methadone dose is less than 40 mg per day. Some patients receiving higher doses of methadone will become unstable if the dose is reduced to this level. If this is a concern, a transfer from high dose methadone to buprenorphine may be considered in rare instances.

### 4.4.2.3 High-dose methadone to buprenorphine transfer

Transfer from high-dose methadone to buprenorphine is possible, but no widely agreed protocol is currently available. Such transfers should only ever be undertaken within a drug and alcohol clinic setting.
4.4.2.4 Transferring from buprenorphine to methadone

A transfer from buprenorphine to methadone should not diminish the stability of the patient. A transfer from buprenorphine to methadone may be appropriate when:

- side effects of buprenorphine are intolerable
- the response to treatment is inadequate.

Patients should be stabilised on daily doses of buprenorphine before transfer to methadone. If possible, reduce the daily buprenorphine dose to 8 mg or less for several days before transfer.

Methadone can be commenced 24 hours after the last dose of buprenorphine. The first dose of methadone should not exceed 40 mg. Patients transferring from lower doses of buprenorphine should receive lower doses of methadone.

As with other patients starting methadone maintenance, take a cautious approach to increasing the dose (see section 4.5.2.2, Titrating methadone dose, on page 33).

4.4.2.5 Transferring from naltrexone to buprenorphine or methadone

Naltrexone is an opioid antagonist used as an adjunct to abstinence from opioids. A switch to methadone or buprenorphine treatment may be appropriate if the patient is lapsing or threatening to lapse into use of illicit opioids.

After a short period on naltrexone, possibly only a few days, the patient loses tolerance to opioids. Consequently, patients transferring from naltrexone should be treated as if they were opioid-naïve unless the clinical circumstances clearly indicate a return to regular, heavy opioid use.

Do not administer methadone or buprenorphine until at least 72 hours after the last dose of naltrexone.

Extreme caution should be exercised with starting doses, which should be no greater than 20 mg of methadone or 4 mg of buprenorphine.

Patients should be warned of the dangers of overdose if they use heroin and/or other drugs at this time, and should be provided with a copy of the Methadone maintenance treatment — essential information booklet and the Methadone overdose card, or the patient information leaflet on buprenorphine.

4.5 Stabilisation

4.5.1 Dose titration

Stabilisation is about titrating the dose against the needs of the individual patient.

Changes in the dose should only be made after the prescriber or nominated clinician assesses the patient.

Assessment should include:

- features of intoxication or withdrawal over the preceding 24 hours (patient’s self-report, examination)
- patient’s perception of dose adequacy and satisfaction with treatment
- patient’s adherence to dosing regimen
- other drug use (patient’s self-report, urine testing)
- side effects and adverse events (including intoxicated presentations and overdoses).

Blood tests to assess plasma levels of methadone or buprenorphine are rarely necessary.

The assessment should be reviewed every two weeks.

4.5.2 Methadone

During the first two weeks of treatment the aim is to stabilise the patient so that they are not oscillating between intoxication and withdrawal. This does not necessarily mean that the patient will reach an optimum maintenance dose in that time. Further dose adjustments may be required after the patient has been initially stabilised.

4.5.2.1 Monitoring during the first two weeks of treatment

Because blood levels of methadone will rise over the first week of dosing, patients should be reviewed at least once, and preferably twice by an experienced clinician (doctor or nurse) in the first week to assess intoxication.

The dosing clinician should observe patients before dosing to check for signs of intoxication (See Appendix I, Intoxication and withdrawal states from commonly used drugs, on page 132).

If intoxication with the prescribed opioid or other drugs is suspected, a doctor or drug and alcohol nurse practitioner should see the patient before the dose is administered.

4.5.2.2 Titrating methadone dose

- Decrease the dose if there are features of intoxication at the time of peak effects (3–4 hours after dosing), or if there are severe or intolerable side effects.
- Do not increase the methadone dose for at least the first four days of treatment unless there are clear signs of withdrawal at the time of peak effects, as the patient will experience increasing effects from the methadone each day.
- Consider dose increments of 5 mg every fourth dose, subject to assessment.
• Total weekly increase should not exceed 15 mg.
• The maximum dose at the end of the first week should typically be no more than 40 mg.
• Warn patients not to drive or operate machinery during periods of dose adjustments.
• Inpatient induction to methadone under specialist management can be more rapid.

4.5.3 Buprenorphine

4.5.3.1 Monitoring

Because of buprenorphine's relative safety in overdose compared to methadone, buprenorphine dosing can quickly reach a level that alleviates withdrawal. Dose stabilisation can be achieved within days rather than weeks. However, during rapid induction the patient should be reviewed daily.

4.5.3.2 Titrating buprenorphine dose

• Buprenorphine doses can be increased quickly and safely in increments of 2–8 mg per day during the first week.
• Dose increases should not be given if the patient reports side effects (eg, nausea, dizziness, agitation, sedation).
• Decrease the dose if there are features of intoxication at the time of peak effects (1–4 hours after dosing), or if there are severe or intolerable side effects.
• Most patients can be stabilised on daily doses of 12–24 mg.
• The maximum daily dose at the end of the first week should be no more than 32 mg.
• There is rarely a reason to prescribe more than 32 mg/day of buprenorphine to any patient.
• To prescribe a dose in excess of 32 mg/day, approval must be sought through the Pharmacotherapy Credentialling Subcommittee.
• Patients should be warned not to drive or operate machinery during periods of dose adjustments.

Because of its long plasma half-life, buprenorphine can be successfully administered on an alternate day or thrice weekly dosing regimen with no increase in reported withdrawal discomfort or reduction in therapeutic efficacy in most patients. The option of alternate day or thrice weekly dosing should be explored with all patients who have been stabilised for two weeks on daily dosing. See section 5.1.2.2 (page 41).

Some patients attempting alternate day dosing may benefit from doses greater than 32 mg, however, there is limited evidence regarding the safety of higher doses, and buprenorphine is registered in Australia with a maximum recommended daily dose of 32 mg.

4.5.4 Dose titration after initial stabilisation

Dose increases are often required and requested by the patient after the second week of treatment for both methadone and buprenorphine. Indications for increasing the dose include:

• inadequate relief of withdrawal for 24 hours
• persistent craving
• continued illicit opioid use.

Patients should be seen by an experienced clinician before any dose increase to determine whether there are any signs of drug (including alcohol) toxicity that would make an increase in dose hazardous. Dose increases should be negotiated with the patient, and only prescribed with the patient's agreement.

Studies with both methadone and buprenorphine show that better treatment outcomes are associated with higher doses. Yet there are individual patients who do well on lower doses and who should not be encouraged to increase their dose.

4.5.4.1 Methadone

Methadone dose increases must be gradual, bearing in mind that it takes up to seven days before new steady-state serum levels are achieved after each dose increase.

Dose changes should occur at intervals of no less than four days, and are usually made no more frequently than weekly.

<table>
<thead>
<tr>
<th>Current treatment</th>
<th>Maximum dose increase per week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methadone 40–100 mg/day</td>
<td>10 mg</td>
</tr>
<tr>
<td>Methadone &gt; 100 mg/day</td>
<td>15 mg</td>
</tr>
</tbody>
</table>

Note: To prescribe a methadone dose above 200 mg/day, approval must be sought through the Pharmacotherapy Credentialling Subcommittee, NSW Health. (Use form given in Appendix M on page 160).

4.5.4.2 Buprenorphine

Buprenorphine dose increases can be more rapid (up to 8 mg per day), but the effective ceiling will be reached quite quickly: there is little evidence of additional therapeutic benefit for dosing above 32 mg/day.

There are reports from some clinicians of patients exhibiting a reduction in therapeutic effect at higher doses due to the increasing antagonist effect of buprenorphine.

To prescribe a buprenorphine dose above 32 mg/day, approval must be sought through the Pharmacotherapy Credentialling Subcommittee, NSW Health (use the form given in Appendix M on page 161).
4.6 Monitoring drug use

Assessing patients’ drug use is:

- essential for safe prescribing and dosing
- a useful guide to progress in treatment
- an aid to clinical decision-making
- part of developing a positive therapeutic relationship

Drug monitoring does not work as well for these purposes if it is used as a basis for punitive actions against patients who continue to use illicit drugs.

The available means of monitoring drug use are the patient’s self-report, urine testing and clinical observation. In future, hair analysis, saliva and sweat analysis may become available. Liver function tests may assist in assessing the impact of alcohol abuse but they lack specificity and sensitivity in detecting moderate alcohol intake.

4.6.1 Self-report

Self-report can be a reliable guide to drug use in settings where no negative consequences result from disclosure. However, there will always be clinical situations in which patients are reluctant to make a full disclosure. Caution should be exercised when making clinical decisions based solely on self-reported drug use. The best information is usually obtained from a combination of self-report, clinical observation and random urinalysis.

4.6.2 Urine drug testing

Urine drug testing is a difficult area over which patients, prescribers and managers disagree. Ideally, it is one method of monitoring the progress of patients during treatment, including detecting extraneous drug use or occasionally detecting methadone or buprenorphine diversion. It should never be used in a punitive way, and overall health and social functioning should not be overlooked as indicators of progress or change.

Urine testing’s usefulness is limited because:

- it may not be a reliable indication of drug use if urination is not observed
- it generally detects drugs used recently, and may not indicate a pattern of use
- supervised urine collection can be demeaning for the patient and staff
- research suggests that urine testing does not reduce drug use
- there are significant financial and resource costs associated with urine drug testing
- false positive and false negative results can occur

Benefits of urine drug testing can include:

- it is an objective form of monitoring when self-report may not always be reliable
- it can provide clear evidence of stability in treatment
- it can be useful for medicolegal purposes.

Although methadone is detected in routine screens, buprenorphine is difficult to detect by routine urine drug screening that relies on chromatography procedures. A consistent indication of whether a patient is consuming buprenorphine as prescribed will not be gained from this type of testing. Enzyme-linked immunosorbent assay (ELISA) or mass spectrometry are techniques that accurately detect the presence of buprenorphine, but these are more expensive and less readily accessible. Because of this, testing for buprenorphine should only be requested when there is a clinical indication.

It is strongly recommended that patients who are receiving takeaway doses are requested to provide a random urine drug screen at least once every two weeks during the first few months of takeaway dosing and monthly thereafter. Although results may not be returned to the prescriber for up to four weeks, they can be used retrospectively to validate clinical decisions. In practice, patients should be asked to provide urine within 24 hours of a request.

4.6.3 Assessing alcohol abuse

Alcohol abuse decreases the safety of methadone or buprenorphine treatment. Liver function tests can be used as an assessment tool in cases of suspected alcohol abuse.

Hepatitis C and alcoholic liver disease produce different patterns of abnormal liver function tests. In alcoholic liver disease, gammaglutamyltransferase (GGT) is likely to be the most strikingly elevated result. Levels of aspartate aminotransferase (AST) exceed alanine aminotransferase (ALT) in most cases and both are less than 500 U/L in the absence of additional complicating factors. In hepatitis C virus infection, ALT is the most prominent abnormality and AST is less than the ALT.

Many patients in opioid treatment have both hepatitis C and alcohol-related liver disease. In these patients, both ALT and GGT are likely to be elevated, but results of liver function tests can be quite variable.

A raised mean corpuscular volume on the full blood count and a raised uric acid level are additional pointers to alcohol abuse. Measurement of breath alcohol may be of assistance acknowledging its limitations.
4.7 Legal requirements for starting methadone or buprenorphine maintenance treatment

4.7.1 Identification

The identity of the patient must be confirmed before treatment commences. Appendix O (page 165) lists appropriate documentation for proof of identity. Some prospective patients may be in chaotic circumstances and have little in the way of proof of identity, but as a last resort they can usually name a contact person who can vouch for their identity. Care in identifying prospective patients is needed, as there have been instances of patients using an alias and being dosed at two different places.

4.7.2 Authorisation

A prescriber must obtain authority for each patient to enter an opioid treatment program by completing a yellow Application for authority to prescribe methadone form, or the lilac Application for authority to prescribe buprenorphine form, from the Pharmaceutical Services Branch (PSB) of the Department of Health and returning it to the PSB, usually by fax to (02) 9859 5170.

A patient must not begin methadone or buprenorphine treatment until approval has been given by the PSB. This will usually be obtained within 24 hours. Confirmation may be obtained by phoning PSB, Methadone Section: (02) 9879 5246.

The authorised maximum dose should not be exceeded without a further application for authority to do so.

An authority to prescribe is valid for a maximum of 12 months.

An exit form (Exit from methadone/buprenorphine treatment, also available from the PSB) must be completed and forwarded to the PSB for each patient discharged from a program or transferred from the care of one prescriber to another.

4.7.3 Prescriptions

A current photograph and/or a detailed written description, as well as a valid prescription, must be forwarded to the clinic or pharmacy where dosing will take place before the person can begin treatment. Do not send the prescription or duplicates of the original to the dosing point with the patient.

A prescription must show:

- the date on which it is issued
- the patient’s name and address
- the daily dose in figures and words (in milligrams, and in millilitres for methadone syrup)
- (for increases and decreases:) both rate and increment change and specific upper and lower limits
- adequate directions for use
- the days on which takeaway doses, if any, are to be provided
- the period for which the dose is to be administered
- the name, designation, address and telephone number of the prescriber.

If a patient is to receive takeaway doses (see chapter 6, page 45), these must also be authorised in writing by the prescriber, either on the prescription or on a separate form attached to it.

The pharmacist would normally only dispense a maximum of two consecutive takeaway doses unless specifically instructed by prescriber.

If the patient is not to commence treatment immediately, the starting date for treatment should be clearly indicated on the prescription.

The dosage must be clear — “increase dose by x mg/day” or “maintain present dose” are not acceptable notations, as the prescriber and dispenser may have different understandings of the current dose.

A prescription is valid for up to six months.

4.7.3.1 Buprenorphine–naloxone prescriptions

Buprenorphine–naloxone prescriptions must name the dispensing point, frequency and date(s) of pick up as well a total dose and daily dose in milligrams. As buprenorphine–naloxone tablets only come in 2 mg or 8 mg tablets, all prescriptions should be for an even number of milligrams to ensure ease of dispensing. The prescription must specify the combination of tablets that will be required (eg, buprenorphine–naloxone 12 mg sublingually daily to be dispensed as 1 x 8 mg and 2 x 2 mg tablets daily).

NSW Health forms used in the administration of the Opioid Treatment Program are given in Appendix M (page 150).
4.8 Dosing location

All patients should commence dosing with methadone or buprenorphine in a well supervised setting. In NSW, this is usually a public or private specialist clinic, but a number of settings may be equally effective if dosing at a specialist clinic creates significant barriers to treatment. Patients may be dosed with methadone or buprenorphine at specialist clinics, community or hospital pharmacies, community or mental health centres and accredited general practitioner/prescriber surgeries, depending on:

- the availability of suitably qualified and trained staff to supervise dosing
- the appropriateness of procedures for methadone or buprenorphine treatment in that setting
- the patient’s suitability for that setting
- the dosing capacity at that setting
- the availability of case management at either the dosing location or elsewhere
- the patient’s financial status
- the practicalities of access to potential dosing locations.

The patient should continue to be dosed in a well supervised setting until assessed as suitable for dosing at a less supervised setting (eg, a retail pharmacy). This may not be possible in areas where access to a specialist clinic is unavailable. Any sites where appropriate supervision can be provided (including retail pharmacies and prescriber surgeries) can be used, particularly for buprenorphine induction.

If a non-clinic dosing site will be used for starting treatment, this should be indicated clearly on the PSB application form for authority to prescribe.

4.8.1 Dosing at a clinic

Specialist clinics (public or private) are generally best placed to manage complex clinical issues and unstable patients. Clinics are usually the most appropriate dispensing points for more vulnerable patients who require greater monitoring due to dangerous drug use or medical/psychiatric conditions.

Community health centres and general hospitals (including outpatient services) can also provide multidisciplinary and highly supervised care on a daily basis.

Patients who behave in a way that disrupts the normal operations of retail pharmacies should be managed in a highly supervised setting.

4.8.2 Dosing at a pharmacy

In locations where there are no public or private clinics, dosing will occur at pharmacies and public hospitals. It is preferable for stable patients to be dosed at retail pharmacies.

The indications of a patient’s suitability for pharmacy dosing are:

- functional social behaviour, with no intoxicated or other unacceptable behaviour at or around the dosing location
- regular, reliable contact with service providers
- no problems in the past six months with alternative dosing locations, including unacceptable behaviour, diversion of doses or deterioration in clinical condition
- the patient agrees to be dosed at a pharmacy and can meet the financial commitment.

After determining where a patient should be dosed, the following practicalities will also need to be addressed and documented:

- the availability of places at the dosing point
- the hours of dosing at the dosing point
- the patient’s time constraints, including work and parenting commitments
- the capability of the patient to travel to the dosing point and the time this will take
- the expectations of the dosing point.

In assessing the patient’s suitability for pharmacy dosing, all clinicians involved in the patient’s treatment (the prescriber, the dosing staff, other case workers) should discuss the issues, and this case discussion should be documented.

Normally it takes about six months from starting methadone treatment and one to three months from starting buprenorphine treatment for the patient to reach the stability required for pharmacy dosing.

Ideally, the pharmacist should be consulted before being recommended to the patient. The patient should meet with the pharmacist, who is ultimately responsible for deciding whether he or she is prepared to dispense methadone or buprenorphine treatment to the patient. The patient’s willingness to be dosed at the pharmacy and agreement to comply with the associated conditions should be documented.

For effective management of patients dosed at community pharmacies, the pharmacist and prescriber or patient’s case worker should communicate regularly (at least every three months). It is advisable for a mechanism to be in place for
the pharmacist to notify the prescriber if the patient misses more than one week of dosing.

The dosing arrangements should be reviewed at least every six months.

Arrangements regarding the transfer of patients from clinics to community pharmacy dosing should always include the capacity to take the patient back to the clinic if significant problems are experienced at the pharmacy.

The financial loss to a clinic incurred as a result of a patient receiving their methadone elsewhere should not be a consideration in the determination of the most appropriate dosing point for a person on methadone.

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**Number of patients at retail pharmacies**

NSW legislation restricts the number of patient’s dispensed methadone or buprenorphine at retail pharmacies to 50 patients in total. This includes patients on detoxification regimens, but not those on prescriptions for buprenorphine–naloxone. This restriction has been applied to ensure that disruption to the local amenity is minimised.
5 Continuing maintenance therapy

Chapter summary

- Daily methadone doses of >60 mg or more are associated with better treatment outcomes in terms of reducing illicit opioid use, criminal activity and HIV risk-taking behaviour and improving retention in treatment.

- In general the upper limit for methadone doses is 150 mg/day; prescribing 200 mg/day or more requires the approval of the Pharmacotherapy Credentialling Subcommittee of the Medical Committee, NSW Health.

- Split (twice daily) methadone dosing may be required for a few patients (eg, pregnant, in pain, rapid methadone metabolisers) and (for a short period) by patients who are experiencing nausea at the time of peak effects.

- Effective buprenorphine dose range for most patients is 12–24 mg/day. Some patients can be satisfactorily maintained on lower doses.

- In general, the upper limit for buprenorphine doses is 32 mg/day; prescribing a daily dose more than 32 mg/day requires the approval of the Pharmacotherapy Credentialling Subcommittee of the Medical Committee, NSW Health.

- Daily dosing is recommended for initial stabilisation of the patient, but many patients can be maintained on alternate-day dosing or even less frequent dosing regimens.

- Review all patients regularly, including those who appear to be progressing well (at least four times a year). A review is a comprehensive reassessment of the patient and progress in treatment.

- Patients should remain in treatment until they achieve their agreed treatment goals. There is no optimal duration of methadone or buprenorphine treatment.

- Case management: people with opioid dependence usually have complex psychosocial and health problems. The Opioid Treatment Program can provide a framework for enhanced care, involving comprehensive assessment, treatment planning, counselling and coordination of other services as required.

- General health of opioid users is often poor and requires care. Hazardous levels of alcohol, tobacco and other drug use are common and merit harm reduction interventions. Psychosocial interventions can add to the effectiveness of the Opioid Treatment Program and should be freely available to all patients (not compulsory).
5.1 Maintenance dose

Tailor the maintenance dose to each patient, and do this in negotiation with the patient. Treatment is most effective when patients know and have some degree of control over their dose.

5.1.1 Methadone maintenance

The research evidence suggests that daily methadone doses in the range 60–150 mg are associated with better treatment outcomes in terms of improving retention in treatment and reducing illicit opioid use, criminal activity and HIV risk-taking behaviour. While most patients will have better outcomes on doses above 60 mg, some patients will respond well to lower doses. It is important that the methadone dose satisfy the patient if they are to benefit from the program.

Trough plasma methadone levels repeatedly below 150–200 μg/L have been nominated in the literature as suggestive of inadequate doses. Such measurements provide helpful information but are rarely necessary. If levels are measured, peak and trough values provide the best information.

5.1.1.1 Upper limit of methadone maintenance doses

In general, the upper limit for methadone maintenance doses is 150 mg.

Pharmacokinetics and clinical response vary between individuals. Some patients may benefit from a daily dose above 150 mg, but a prescriber should increase the dose beyond 150 mg only after careful consideration. Seek (and document) a review by the clinical team (in the case of a clinic) or a second opinion from a drug and alcohol medical specialist when doses are to be raised above 150 mg. High-dose methadone (200 mg/day or above) has been linked to a low but significant risk of cardiac arrhythmias (torsade de pointes), the risk being greatest in those with an underlying prolonged QT interval. The risk may exist at lower doses of methadone in those with underlying cardiac disease, a family history of cardiac disorders and in those on multiple concomitant medications. These patients should have a routine electrocardiogram performed at initial assessment.

5.1.1.2 Split dosing

There are a few individuals who metabolise methadone rapidly (ie, patients in whom peak methadone levels are adequate but levels are not maintained adequately). These patients may require dosing twice a day (split dosing).

Restrictions on prescribing methadone doses of 200 mg/day or above

Prescribing a daily methadone dose of 200 mg or more requires a second opinion from an drug and alcohol medical specialist.

An application form for approval to prescribe methadone doses above 200 mg is available in Appendix M (page 160).

The application must be supported by:

- a second opinion from a prescriber who is a Fellow of the Chapter of Addiction Medicine, or a prescriber of equivalent training and experience approved by the Pharmacotherapy Credentialling Subcommittee
- an ECG giving corrected QT intervals (QTc), measurements of trough blood levels of methadone and observations 2–3 hours post-dose
- details of current methadone dose, the number of takeaway doses prescribed, current medications, details of a recent urine drug test, whether the patient has chronic pain and whether alternative methods of treatment have been addressed. See section 3.12.6 (page 24) regarding release of information consent forms and the Prescription Shopping Line
- details of the dose applied for and the reason for the increased dose.

A similar restriction applies to prescribing more than 32 mg/day of buprenorphine.

Split dosing may also be useful:

- early in treatment, when patients may exhibit a low tolerance to the nauseating side effects of methadone
- for pregnant patients who experience persistent nausea
- for patients with chronic pain.

In such cases, split dosing is only required for a short time and can be discontinued within four weeks.

Obtain and document a second opinion from a drug and alcohol medical specialist before:

- instituting split dosing
- continuing split dosing beyond four weeks
- authorising one or more of the split doses to be taken away.

Buprenorphine maintenance dosing never needs to be more frequent than once a day.

5.1.2 Buprenorphine maintenance

The effective dose range for most patients is 12–24 mg/day. However, there is significant individual variation in dose requirement. While a dose of 4 mg/day is unlikely to be
effective, some patients can be satisfactorily maintained on 8 mg/day.

5.1.2.1 Maximum maintenance dose

The approved maximum daily dose of buprenorphine is 32 mg. To prescribe a daily dose in excess of 32 mg/day, approval must be sought from the Pharmacotherapy Credentialling Subcommittee (see form in Appendix M on page 161).

5.1.2.2 Less-than-daily dosing

Daily dosing is recommended for the initial period of stabilisation. Evidence suggests that a significant proportion of patients on buprenorphine can be adequately maintained by receiving a dose every alternate day and some even every third day. Patients can be offered the alternative of second daily dosing at 1–2 weeks.

A trial of less-than-daily dosing is encouraged for all patients who have been stable on buprenorphine for at least two weeks. Stability is represented by a steady dose requirement and no evidence of intoxication or dangerous use of other drugs in that time.

Some patients may be reluctant to trial less-than-daily dosing because of a perception that less frequent doses would be less effective. They should be encouraged to consider the advantages of less frequent attendance for dosing, and reassured that they can return to daily dosing if a trial of less-than-daily dosing is unsatisfactory.

Due to the longer duration of action at a higher dose the benefits of less-than-daily dosing include reduced time spent in travel to the dispensing point, more time to undertake activities that promote improved social functioning and less congregation of patients around dosing points. However, not all patients are suited to less-than-daily dosing. Some experience increased cravings or withdrawal before their next dose is due, or intoxication on dosing, and are better suited by daily dosing.

To trial less-than-daily dosing:

- Check that the patient is stable on the daily dose administered over the preceding week or two. Contraindications to less-than-daily dosing:
  - irregular attendance for dosing
  - intoxicated presentation for dosing
  - continuing frequent or regular illicit opioid use
  - concerns over other drug use (eg, alcohol, benzodiazepines)
  - patient requires close observation and monitoring (eg, dual diagnosis, behavioural problems, pregnancy, unstable drug use)
  - patient wants to continue attending daily.

- Offer the patient the opportunity to trial less-than-daily dosing. Explain that higher doses lead to longer duration of action without increased opioid effect in the long term. Explain that increased sedation may be a problem in the first few days, but that this should pass. Document this discussion and its outcome in the patient notes.

- Since there is wide variability in individual responses in terms of duration of action and toxicity with higher doses of buprenorphine, patients will need to be monitored closely during this time.

- Review the patient after the first week or two of less-than-daily dosing.

### Buprenorphine dosing regimens

<table>
<thead>
<tr>
<th>Daily</th>
<th>Alternate day</th>
</tr>
</thead>
<tbody>
<tr>
<td>■ Standard initiation regimen.</td>
<td>■ Patient attends for dosing every second day.</td>
</tr>
<tr>
<td>■ Suitable for patients who experience withdrawal between or intoxication on less-frequent dosing.</td>
<td>■ This is a simple regimen, but it means that the patient does not attend for dosing on the same days of the week every week, which can lead to dosing errors.</td>
</tr>
<tr>
<td>■ The 48-hour dose is initially set at twice the patient's 24-hour dose, up to a limit of 32 mg per dose.</td>
<td>■ If the patient reports features of intoxication from buprenorphine during its peak effects, reduce the dose by 4–8 mg.</td>
</tr>
<tr>
<td>■ If the patient reports features of withdrawal or drug cravings during the 48 hours between doses, increase the dose by 4–8 mg, up to a maximum of 32 mg.</td>
<td>■ If the patient reports features of withdrawal or drug cravings during the 48 hours between doses, increase the dose by 4–8 mg, up to a maximum of 32 mg.</td>
</tr>
</tbody>
</table>

| Four times a week | ■ Patient attends for dosing on four set days of the week, receiving three 48-hour doses and one 24-hour dose. Setting the attendance days may reduce the chance of dosing errors. |
| Three times a week | ■ Titrates the 48-hour doses as for the alternate day regimen. |

■ The 72-hour dose is initially set at 32 mg or three times the patient's 24-hour dose, whichever is the lower. |

■ Titrates the doses as for the alternate day regimen. |
• To assess the adequacy of alternate daily dosing patients should be asked:
  — about the number of cravings and likelihood of illicit use
  — whether they were as comfortable on the second day as the first
  — how well they slept on the second night.

Most patients will be successfully maintained on doses of 32 mg every two or three days. The need to prescribe higher maintenance doses should be minimal. If higher maintenance dose prescribing continues beyond six months it should prompt a second opinion review.

Contraindications to persisting with less-than-daily dosing:
• intolerance of side effects or persistent sedation after dosing
• concerns about stability (continuing use of illicit opioids, issues with mental health or social situation)
• patient wishes to return to single day dosing
• prescriber wishes to supervise other psychotropic medications to enhance compliance.

5.2 Treatment review
Review all patients regularly, including those who appear to be progressing well. The frequency of patient review will be determined by the stability of the patient, but all patients should be reviewed at least four times a year by an experienced clinician. This is a legal requirement that, whenever a prescription for methadone is provided or renewed, the prescriber personally assesses the patient.

Patients not progressing well in treatment will benefit from more frequent intervention.

The review of treatment progress should document:
• any patient requests, current issues or concerns
• treatment mechanics, such as dosing location or take-away doses
• adequacy of methadone/buprenorphine dose and any pharmacological issues (side effects, or interactions)
• recent drug use — prescribed and other (including alcohol and tobacco)
• physical and psychological health
• social functioning
• behaviour with a risk of HIV, hepatitis B and hepatitis C infection (test liver function and virology if indicated)
• renewal of prescription
• plans for the patient’s treatment program, including strategies to enhance the patient’s capacity to withdraw from the opioid treatment program.

5.2.1 Duration of maintenance treatment
Regular reviews help determine the need for continued treatment. Patients should remain in treatment for the minimum time it takes to achieve their agreed treatment goals. There is no optimal duration of methadone or buprenorphine maintenance, but removing people from treatment too early may result in very poor outcomes, including high rates of relapse into illicit opioid use and a consequent increased risk of overdose. Setting an arbitrary duration of treatment and withdrawing treatment at that endpoint is not recommended.

5.3 Case management
People with opioid dependence usually have complex psychosocial and health problems, which have to be addressed if treatment of their opioid dependence is to succeed. The Opioid Treatment Program can provide a framework for enhanced care, involving comprehensive assessment, treatment planning, counselling and coordination of other services as required.

When assessing and reviewing patients, clinicians providing opioid treatment need to consider the broader picture of each patient’s health and progress. A case management approach should be offered to all patients. The following ancillary services should be provided either within the opioid treatment program or by referral:
• Crisis intervention: Patients often have urgent problems. Collaborative care with key services such as mental health, Department of Community Services and Justice Health is often necessary.
• Medical services (preventive, early intervention and treatment): People with opioid dependence have greater health risks and morbidity than the general population. All drug and alcohol professionals should have a level of expertise in identifying medical problems associated with opioid use. Hepatitis B and C, HIV, and bacterial infections including bacterial endocarditis and osteomyelitis are not uncommon and should be sought in assessment processes. Patients need to be provided timely and effective referral to medical services for their needs. Treatment for concurrent psychiatric conditions is not uncommon.
• Community services: Multiple social problems are common among opioid dependent people. Providing vocational, financial, accommodation and family assistance contributes positively to the progress of their treatment.
• Counselling (brief, supportive, and problem-oriented): Counselling should not be mandatory within the Opioid Treatment Program, but access to counselling does appear to add to the effectiveness of methadone or buprenorphine treatment for patients with current life problems. Cognitive-behavioural therapies (such as motivational interviewing), relapse prevention counselling, and social skills training are some of the counselling approaches often employed.
All ancillary services should be provided on the basis that the patient freely wants to be involved.

5.4 Maintaining health

5.4.1 General health issues in opioid dependent people

Some individuals can maintain a normal lifestyle while regularly using opioids, but most suffer health problems related to their drug use. Diet and personal hygiene can be compromised, and this leads to increased susceptibility to infections and to a sense of ill health. Sharing of injecting equipment exposes individuals to risk of bacterial infections and to infection with bloodborne viruses such as HBV, HCV and HIV. Patients who present for assessment for methadone or buprenorphine treatment should be encouraged to see their general practitioner for a full medical check-up, or should be evaluated fully by their drug and alcohol doctor, twice yearly.

5.4.2 Alcohol and tobacco use

Many individuals who use opioids also smoke tobacco and a smaller percentage use alcohol at harmful or hazardous levels. It is not appropriate to ignore these other drugs, as the physical harm caused by their excessive use is greater than that caused by opioid use. Smoking cessation strategies can be effective in this population and patients should be encouraged to stop smoking while in treatment. Alcohol dependence or hazardous drinking should also be addressed actively. The risk of liver damage is increased when alcohol use combines with hepatitis C infection.

Further information

Effective psychotherapies


Cognitive–behavioural therapy:

“In behavioural and cognitive psychotherapies the therapist and the client work together to:

■ develop a shared understanding of the client’s problem.
■ identify how these affect the client’s thoughts, behaviours, feelings and daily functioning.

Based on the understanding of each client’s individual problems the therapist and the client will then work together to identify goals and to agree to a shared treatment plan. The focus of therapy is to enable the client to generate solutions to their problems that are more helpful than their present ways of coping. This often involves the client using the time between therapy sessions to try things out.”


Motivational interviewing:

“Motivational interviewing is a directive, client-centered counselling style for eliciting behaviour change by helping clients to explore and resolve ambivalence. Compared with nondirective counselling, it is more focused and goal-directed . . . Motivation to change is elicited from the client, and not imposed from without.”


On the web: Motivational interviewing <http://www.motivationalinterview.org/>

Further information


5.4.3 Other drug use

Use of other drugs of dependence such as cannabis, benzodiazepines and psycho stimulants such as amphetamines or MDMA (“Ecstasy”), should be enquired about in any full assessment. Patients should be provided information on the risks of their drug use and offered assistance in reducing use of these agents.

5.4.4 Psychosocial support

Providing adequate medical care and counselling services for those patients who want them leads to better retention rates and outcomes. Structured, evidence-based interventions include motivational interviewing, aggressive case management, cognitive behavioural approaches such as relapse prevention and skills training, and supportive, expressive therapy.

Psychosocial interventions that add to the effectiveness of an opioid treatment program should be freely available to all patients and not compulsory. They should be individualised according to patient needs, based on a supportive therapeutic alliance, delivered by appropriately trained clinicians, and well integrated into the overall service delivery system.

Further information

6 Takeaway doses

Chapter summary

- Methadone and buprenorphine are usually dispensed to patients for immediate consumption under supervision. Providing takeaway doses has risks (illicit use, diversion to or accidental consumption by others, loss of contact with patient) and benefits (patient and dispenser convenience, promotion of patient responsibility, incentive to progress in treatment).

- Takeaway doses should be provided only after a careful assessment of the patient’s stability and reliability, and never if there is concern that they will be misused.

- In general, patients receiving takeaway doses should be observed once every three days.

- Many patients on buprenorphine can be treated with alternate-day, four-day-a-week or three-day-a-week dosing regimens that greatly reduce the need for takeaway doses.

- If takeaway doses of buprenorphine are to be given, combined buprenorphine–naloxone is to be used unless clinically inappropriate (eg, the patient is pregnant or sensitive to naloxone).

- Transfer to buprenorphine–naloxone and being eligible for takeaway doses is normally a necessary step towards being able to receive weekly, fortnightly or monthly scripts.

- Patients receiving takeaway doses of buprenorphine–naloxone must be informed that injecting buprenorphine–naloxone is likely to precipitate withdrawal in opioid dependent people.

- Providing regular takeaway doses requires the prescribing doctor to be satisfied that the patient is reliable and stable. This should be evaluated as per the Suitability for takeaway doses assessment form (Appendix L, page 148):
  - no hazardous use of opioids and other drugs (including alcohol)
  - improved social functioning
  - compliance with program requirements
  - a prior history of responsible use of takeaway doses
  - able to provide adequate storage arrangements for takeaway doses
  - understanding the potential risks to children of accidental ingestion.

- Absolute contraindications to takeaway doses:
  - repeated intoxication on presentation for dosing at the clinic/pharmacy
  - the patient has a child or children living in their household, and there are concerns that the child/children may be at risk of harm
  - current chaotic and unpredictable behaviour
  - assessed as at risk of self-harm
  - current hazardous use of drugs (including benzodiazepines or alcohol).

- In remote areas, opioid treatment services may have to develop a policy on takeaway doses that acknowledges the impracticality of 7-day-a-week on-site dosing for some patients. Such a policy must address the objective of minimising the diversion and injection of methadone or buprenorphine. Absolute contraindications cannot be ignored.

- Reasons for going outside guidelines should be documented.
Chapter summary

- **Time in treatment and methadone takeaway doses:**
  - First 3 months of treatment: no takeaway doses other than in the most exceptional circumstances.
  - 3–5 months in treatment: observe the patient every second day. A maximum of two takeaway doses may be provided per week.
  - 6–8 months in treatment: observe the patient every third day. A maximum of three takeaway doses may be provided per week.
  - 8–12 months: observe the patient every third day. A maximum of four takeaway doses may be provided per week in no more than two consecutive doses.

- **Time in treatment and buprenorphine–naloxone takeaway doses:**
  - First 3 months of treatment: no takeaway doses.
  - As with methadone, increased takeaway doses are only allowed if the patient demonstrates stability on the current program.
  - 3–4 months in treatment: a maximum of two takeaway doses for four weeks.
  - 4–5 months in treatment: a maximum of four takeaway doses for four weeks (no more than two consecutive).
  - 6–8 months in treatment: weekly scripts for at least 3 months. Weekly prescriber reviews.
  - 8–12 months: fortnightly scripts for at least 3 months, fortnightly prescriber reviews.
  - 12+ months: 28 day scripts if maintaining a high level of stability at monthly prescriber reviews.

- Takeaway doses should be the same dosage as those consumed under supervision at the clinic or pharmacy.

- Takeaway dose arrangements are not to be automatically transferred when patients change prescribing doctors.

- The prescribing doctor is to provide the clinic or pharmacy with written authorisation (which should be in the prescriber’s own handwriting and signed) for takeaway doses. This must be attached to, or incorporated in, the current prescription and must specify the date or (when regular takeaway doses are provided) the days of the week on which the patient is to receive takeaway doses.

- Takeaway doses are to be given to patients on the day before the scheduled absence from the dosing point. The patient must be advised of the dangers of misusing the dose, the hazards of using it in combination with other drugs, and its toxic potential if taken by a child or anyone not tolerant of opioids.

- If a patient reports that takeaway doses have been lost, stolen or damaged, a replacement should not be dispensed unless there is a medical indication to do so (such as to prevent withdrawal symptoms in pregnant patients). If medically indicated, replacement doses should be carefully titrated against the observed clinical condition of the patient. Replacement doses are not usually full doses. Careful assessment and monitoring are required to ensure that the patient is not overdosed. Regular loss of takeaway doses (for any reason) suggests that a return to supervised dosing is indicated.
6.1 Risks and benefits of providing takeaway doses

Methadone and buprenorphine are usually dispensed to patients for immediate consumption under supervision. This reduces the risks of unsafe dosing or diversion of the dose to an illicit purpose. However, providing takeaway doses to patients can have advantages if properly managed.

<table>
<thead>
<tr>
<th>Risks</th>
<th>Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>■ Patient may deliberately administer the dose to another person. Ingestion of methadone can be particularly dangerous for children. Even the smallest amount can be fatal.</td>
<td>■ Takeaway doses free the patient from the need to attend the clinic or pharmacy daily, saving time and travel expense, and simplifying the patient's participation in education, training, employment and home duties. This objective is also achieved by moving to a less frequent dosing regimen with buprenorphine treatment (which may be a better alternative than takeaway doses for some patients).</td>
</tr>
<tr>
<td>■ Patient may divert the dose to another person.</td>
<td>■ Takeaway doses emphasise and promote patients' responsibility for their own treatment.</td>
</tr>
<tr>
<td>■ Another person, such as a child, may inadvertently consume the dose. The risk of accidental overdose is much greater for children or people who have not developed a tolerance to opioids.</td>
<td>■ Providing takeaway doses can reinforce compliance with program goals and objectives.</td>
</tr>
<tr>
<td>■ Patient may attempt to inject the dose. Injecting methadone syrup or buprenorphine tablets can cause venous damage, emboli and tissue necrosis and (if needles are shared) transmission of infectious diseases including HIV, hepatitis B and hepatitis C. Injecting buprenorphine or combined buprenorphine–naloxone can precipitate a withdrawal reaction in an opioid dependent patient.</td>
<td>■ Providing takeaway doses can promote a trusting relationship between staff and patients.</td>
</tr>
<tr>
<td>■ Patient may combine the dose with other drugs, increasing the risk of overdose.</td>
<td>■ Patients with takeaway doses are more able to engage in normal day to day activities including work commitments, education, community activities and parenting.</td>
</tr>
<tr>
<td>■ Patient may not take the dose at the specified time (risking withdrawal), perhaps choosing to combine doses for an enhanced effect (risking overdose).</td>
<td>■ The workload for the dispenser is reduced.</td>
</tr>
<tr>
<td>■ Patients seen less frequently may be less likely to seek help if they experience problems, or may present later.</td>
<td>■ The number of patients congregating at dosing points is reduced.</td>
</tr>
</tbody>
</table>

6.2 Providing takeaway doses

It is the responsibility of the Area Health Services to provide sufficient dosing sites for patients who are unsuitable for takeaway doses and the prescribing doctor's responsibility to arrange for individual patients to be dosed at these sites. Ideally, all patients should have access to on-site dosing seven days a week, with no patient receiving takeaway doses simply because of lack of access. There are instances (in remote areas) where this cannot be achieved.

If patients have particular work or family commitments, are chronically ill, or need to travel long distances to the clinic or pharmacy, it is better to adopt more flexible, user-friendly dosing hours (eg, opening earlier and closing later to accommodate those working) or to offer pharmacy pick-ups than to provide takeaway doses.

Takeaway doses can be authorised only by the prescribing doctor, but should be discussed with the clinician(s) or pharmacist with whom the patient has more regular contact. Prescribers should be aware that making up and dispensing takeaway doses takes some time, and should avoid sudden (non-collaborative) approval of takeaway doses or changes to days or dosage.

While it is recommended that patients be seen once every three days while in an opioid treatment program, evidence that this optimises outcomes is sparse. It is generally not appropriate to dispense more than two days supply of takeaway doses. There are a few specific exceptions to this rule:

- **Travel**: a patient who is travelling or going on holiday may have a reasonable case for an extended period of takeaway dosing.
- **Family crisis**: a death or serious illness in the family may require the patient to be absent from the dosing site for an extended period. Temporarily transferring the patient to another opioid treatment program may be a better option than takeaway doses, even if this is more difficult to arrange.
• Severe illness confining the patient to home for a period of time. While home dispensing may be possible in many situations this cannot be sustained and takeaway dosing may be the only workable option. Always consider a community pharmacy dispensing option first.

• Disasters, either local (eg, flooding, fire) or more general (eg, pandemic influenza) may render standard practice in relation to takeaway dosing unworkable. In these instances providing a number of takeaway doses may be necessary. This should be clearly documented.

6.3 Takeaway doses and buprenorphine

Many patients on buprenorphine can be treated with alternate-day, four-day-a-week or three-day-a-week dosing regimens that greatly reduce the need for takeaway doses. When a patient on buprenorphine is to be given takeaway doses, combined buprenorphine–naloxone should be used, provided that there are no clinical contraindications to the combination (such as pregnancy or hypersensitivity). Eligible patients will be switched from buprenorphine to the combination product, and provided with progressively more doses to take without direct supervision, with some (a minority) reaching the stage of picking up medication monthly.

Patients new to buprenorphine or buprenorphine-naloxone will be required to demonstrate three month’s stability on supervised dosing before being considered eligible for takeaway doses.

6.4 Determining suitability for regular takeaway doses

The decision to prescribe doses of methadone or buprenorphine for regular unsupervised consumption must be based on a clinical assessment of the stability of the patient and the likelihood of the takeaway doses improving their lifestyle without impairing their clinical progress.

Going outside these guidelines is a clinical decision that requires documentation. Prescribers are advised to use the Suitability for takeaway doses assessment form (See Appendix L on page 14B), or their own variation of this form, to justify clinical decisions.

6.4.1 Absolute contraindications to takeaway doses

6.4.1.1 Repeated intoxication on presentation for dosing at the clinic/pharmacy

Repeated intoxication on presentation for dosing within the previous three months is an absolute contraindication to providing takeaway doses.

If a patient presents to a dosing site intoxicated, takeaway doses are not to be provided on that day.

6.4.1.2 Child welfare issues/Department of Community Services involvement

The highest priority is to be given to the safety of children residing in the patient’s household.

Any doubts about the ability of the patient to provide adequate living conditions to offer a safe environment for children aged 0–16 should result in takeaway doses not being approved. These doubts should be reported under the mandatory reporting requirements to the Department of Community Services (DOCS) for investigation (Children and Young Persons [Care and Protection] Act 1998 [NSW]):

Public Area Health Service prescribers

• Protecting Children and Young People: NSW Health PD2005_299
• Frontline Procedures for the Protection of Children and Young People NSW Health (2000)
• Children and Young Persons (Care and Protection) Act 1998 (NSW).

Private sector prescribers

• Section 24 of the Children and Young Persons (Care and Protection) Act 1998 (NSW)
• Private prescribers that work in an incorporated practice that provides services wholly or partly to children are also required to comply with section 27 and 248 of the Children and Young Persons (Care and Protection) Act 1998 (NSW).

All prescribers of opioid treatment are required to comply with the information sharing protocol developed between NSW Health and DOCS on assessing potential risk of harm to children less than 16 years of age under the Children and Young Persons (Care and Protection) Act 1998 (2006) (NSW).

All relevant reporting policies and legislation should be followed in accordance with the conditions imposed on a prescriber’s authority to prescribe under the poisons and therapeutic goods legislation. DOCS may contact prescribers and other health professionals to request information relating to the safety, welfare and wellbeing of a particular child or young person. Prescribers must comply with all reasonable requests for information from DOCS regarding a child or children at risk. DOCS’ preferred means of gaining information from Area Health Services is a request for information under Section 248 of the Children and Young Persons (Care and Protection) Act 1998 (NSW).
In reviewing the appropriateness of takeaway doses for patients residing with children, the prescriber should always include dialogue with the dispenser (in most cases, a pharmacist). The dispenser may occasionally observe children with the patient and may be able to provide additional information as to the stability of the patient. The outcome of any review, including dialogue with the dispenser should be documented. See section 6.4.5 (page 51) and section 7.14 (page 76) for additional information on child safety.

6.4.1.3 Current chaotic and unpredictable behaviour

A patient presenting with chaotic or unpredictable behaviour, for whatever reason, is not stable by definition. Takeaway doses should not be provided until stable behaviour has been demonstrated for at least three months.

6.4.1.4 Assessed risk of self-harm

Indications of suicidal thoughts or self-harm behaviours are to be taken as signs of instability and takeaway doses are not to be provided. A period of at least three months of stability should occur before the issue of takeaway doses is reconsidered.

6.4.1.5 Current hazardous use of drugs

People who are regularly injecting drugs, and/or are dependent on alcohol, benzodiazepines, or stimulants are not suitable for regular takeaway doses.

It is critical that assessment of drug injecting behaviour includes a physical examination for signs of injecting. In some cases, such as recent overdose or signs of injection, the clinic or dosing point may implement an automatic “no takeaway” policy until the patient is reviewed by the prescribing doctor.

Evidence of injecting should result in takeaway doses being refused until such time as the prescriber is convinced that the patient is able to use takeaway doses appropriately.

6.4.2 Determining stability — drug use indicators

All patients should be assessed regularly to determine their drug use pattern and psychosocial stability. Takeaway dosing should only be offered when there is evidence of stability in these areas. Increasing the number of takeover doses should only be allowed when there is evidence of ongoing improvement and stability.

6.4.2.1 Current drug use

The issue of current illicit drug use can create problems for some prescribers. It is a question of relative harm. For example: is use of cannabis on a regular basis a contraindication to takeaway doses if it is the only illicit drug being used? If a patient states that he used psychostimulants or heroin once in the past month should this be reason to cease takeaway doses for a period if doing so risks destabilising the patient in other ways?

There is no firm answer to these questions and different specialists and prescribers take different positions on this issue. Ultimately it is a question of clinical judgment based on risks and benefits and any local policies that may apply at public or private clinics.

If:

- the patient has diverted doses within the last three months
- there is evidence of recent (past three months) injection of drugs
- there is evidence (ie, self-report) of current hazardous use of drugs (including benzodiazepines, stimulants, alcohol or illicit substances)
- the patient has missed doses in past three months

... then the stability of the patient’s drug use must be questioned.

6.4.2.2 Unstable drug use

Drug use can be considered unstable if any of these criteria are met:

- use of heroin, amphetamines and or cocaine on > 4 occasions per month
- daily average alcohol intake > 60 g
- high risk episodic drinking of alcohol
- episodic or regular intoxication with benzodiazepines.

In assessing whether the use of alcohol or other drugs is hazardous, consider whether it presents a danger of overdose.

If takeaway doses are to be provided, the prescribing doctor must be satisfied that the combination of drugs consumed does not increase the risk of overdose, instability, poor health and social functioning or other harm. In particular, the prescribing doctor must be sure that the patient can ensure the safety from accidental overdose of children in a household.

6.4.2.3 Determining the level of drug use

Drug use should be assessed by:

- At least three random urine tests in the four weeks before providing takeaway doses. Each additional unsupervised dose requires additional supportive random urine test results (when takeaway doses are contingent on not using other drugs, self-report is not of value in assessing drug use).
• Clinical examination (inspection of veins, signs of alcohol abuse).

• Reported behaviour on presentation for dosing (incidents of missed doses or intoxicated presentation). The self-report of the patient should be confirmed with staff at the dosing point.

• Liver function tests can be useful in cases of suspected alcohol abuse. Elevated gammaglutamyltransferase (GGT) is unusual in chronic viral hepatitis, and suggests excessive drinking.

• Evidence of doctor shopping from the Health Insurance Commission or a Pharmaceutical Benefits Scheme safety net entitlement card.

A reduced number of takeaway doses (maximum of two per week) may be available for patients meeting all other measures of stability and who are using heroin, amphetamines or cocaine once per week or less.

Refusal to provide random urine samples should be considered as a factor against allowing continued takeaway doses.

6.4.3 Determining stability — psychosocial assessment

A patient's social, personal and physical functioning and suitability for unsupervised dosing is indicated by a range of factors.

6.4.3.1 Attendance at regular clinic review appointments

Successful treatment outcomes are related to treatment compliance. The ability to attend appointment times for scheduled clinical reviews is an important indicator of patient engagement. In general, there should be regular attendance at scheduled appointments with the prescriber and case manager (at least three with prescriber in the three months before commencement of takeaway doses).

6.4.3.2 Acceptable behaviour at prescriber practice and dosing site

"Acceptable behaviour" means no aggressive or threatening behaviour towards staff or others for at least three months prior to considering takeaway dosing. Incidents of violence are grounds for suspension from the opioid treatment program or for other sanctions (such as transfer to another prescriber or dosing site).

If a patient demonstrates aggressive behaviour in the private sector (ie, community pharmacy or general practice) then transfer back to an Area Health Service is appropriate.

6.4.3.3 Current evidence of employment and/or educational activity

Employment or educational commitments are usually a sign of improved stability and should be strongly encouraged. Documented evidence of these activities should be sighted as part of the assessment for takeaway dosing.

6.4.3.4 Stable accommodation

Having stable accommodation is important to psychosocial functioning. If a patient does not have stable accommodation, special care should be taken and takeaway doses should be considered only in special circumstances.

Accommodation can change over time, and reviews of takeaway doses should consider any changes of accommodation that may occur between reviews.

6.4.3.5 Stable mental health

Ongoing reviews of mental health should be part of normal scheduled medical reviews of patients. Symptoms of depression and anxiety are not contraindications to takeaway dosing unless they are severe, but it is important to ensure that appropriate treatment or referrals are made to deal with these mental health issues.

Patients with any symptoms of psychosis or severe depression or anxiety should not be given takeaway doses until these issues are under control.

6.4.3.6 Patient reports continuing improvement in psychosocial functioning

Research has shown that participation in an opioid treatment program usually results in major improvements in a patient's social, personal and physical functioning. This is reflected in stabilisation of social relationships, work and other activities. This will usually be reported by the patient. If a patient is not reporting improvement in psychosocial functioning this factor should be investigated further before takeaway doses are considered.

6.4.3.7 No criminal activity

Several public and private clinics have developed memorandums of understanding regarding issues related to amenity (patients causing a general public nuisance around or near clinics). In these cases police may report socially disruptive behaviours of patients associated with dosing to a clinic. If so, the information should form part of the assessment of the appropriateness of continuing takeaway dosing.

6.4.3.8 No significant destabilising life events

Patients who receive or are being assessed for takeaway doses may experience traumatic events such as the death of...
a relative, legal action, or relationship problems. Each of these has a potential to destabilise a patient. Life events that have taken place between reviews should be considered in discussing takeaway dosing.

6.4.4 Access issues

So long as there are no contraindications, takeaway doses above and beyond those normally recommended may be provided if one or more of the following conditions is demonstrated:

- work commitments interfere with daily attendance at a dosing site
- travel hardship — remote area, large distances and or prohibitive cost of travel to a dosing site make daily attendance a hardship
- education commitments interfere with daily attendance at a dosing site
- parenting commitments interfere with daily attendance at a dosing site
- other factors (which should be documented) interfere with daily attendance at dosing site.

It is important that the prescriber sight evidence of the condition justifying increased takeaway doses. This may be in the form of group certificate, pay statement, or a letter from a general practitioner, pharmacist or other agency or person who can confirm the social circumstances of the patient.

In remote areas, opioid treatment services may have to develop a policy on takeaway doses that acknowledges the impracticality of 7-day-a-week on-site dosing for some patients. Such a policy must address the objective of minimising the diversion and injection of methadone and buprenorphine. Absolute contraindications cannot be ignored.

Reasons for going outside guidelines should be documented.

6.4.5 Children at risk of harm

Prescribers are to give the highest priority to ensuring the safety of children.

Takeaway doses may be accidentally ingested by children or deliberately administered to them. If there are children in the patient’s household, consideration needs to be given to the type of medication, the dose and the frequency of review of takeaway dosing.

In households where there are children aged under 16 years, a detailed assessment should be undertaken, including communication with other agencies who may be involved in patient management.

For patients on higher doses, particularly methadone, particular care should be taken in advising of the importance of safe storage and warning of the dangers of methadone.

Patients with children in the household should be reviewed at least every three months. Any indication of instability, significant change in clinical situation or report from DOCS of issues in relation to children in the household should prompt a review of takeaway dosing arrangements.

If a prescriber is notified or receives a request for information from DOCS in relation to children in the household, the prescriber should assess the most recent treatment review and determine whether another review is necessary. In reviewing the appropriateness of takeaway doses, the prescriber should always include dialogue with the dispenser (in most cases, a pharmacist). The dispenser may occasionally observe children with the patient and may be able to provide additional information as to the stability of the patient. The outcome of any review, including dialogue with the dispenser should be documented. The prescriber should always err on the side of caution if prescribing takeaways when there is any child safety issue.

It is recommended that prescribers consider prescribing buprenorphine–naloxone for new patients who have young children in their household, as this medication is less dangerous to children than methadone. For existing methadone patients, it is strongly suggested that prescribers consider transferring patients onto buprenorphine–naloxone. The potential for destabilising patients by a change in medication must be considered and discussed with the patient before action is taken.

Prescribers must ensure that the patient is advised on adequate and safe storage of takeaway doses:

- Keep out of reach of children
- Store in containers with a child-resistant cap
- Store in a high cupboard — a locked cupboard if possible
- Do not store beside your bed
- Do not store in the fridge
- Do not take methadone or buprenorphine in front of children, particularly children aged under six years.
- Clinicians should clearly document their advice to patients about the dangers of methadone and buprenorphine and the importance of safe storage.
6.5 Time in treatment and allowable takeaway doses

Access to takeaway doses should be granted conditionally and gradually increased if and when the patient demonstrates continuing stability and negative urine screens for opioids.

There is a difference in the rates at which takeaway doses are allowed for buprenorphine and methadone patients. This is in recognition of the significantly greater toxicity and pharmacological availability of methadone following oral ingestion. Diverted doses of methadone or unsafely stored takeaway doses of methadone have a far greater potential to lead to fatal consequences than buprenorphine, which is poorly absorbed if swallowed and which is less likely to produce fatal respiratory depression. By requiring a longer period of demonstrated stability on methadone it is believed that fewer adverse consequences will be experienced.

Time in treatment in another opioid treatment program (including the Justice Health system) should only be counted if the prescribing doctor has full information about the patient's treatment and progress in that program. Time in treatment within the Justice Health system does not necessarily provide evidence of stability within a community setting.

<table>
<thead>
<tr>
<th>Stage of treatment</th>
<th>Methadone (and occasionally buprenorphine)</th>
<th>Buprenorphine–naloxone</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–3 months</td>
<td>No access to takeaway doses other than in the most exceptional circumstances.</td>
<td>No takeaway doses.</td>
</tr>
<tr>
<td>3–4 months</td>
<td>Observe the patient no less frequently than every second day and provide a maximum of two takeaway doses per week (not consecutive) if stability has been demonstrated and contraindications are absent.</td>
<td>Observe the patient no less frequently than every second day and provide a maximum of two takeaway doses per week (not consecutive) if stability has been demonstrated and contraindications are absent.</td>
</tr>
<tr>
<td>4–5 months</td>
<td>As above.</td>
<td>Observe the patient no less frequently than every third day and provide a maximum of four takeaway doses per week if stability has been demonstrated and contraindications are absent.</td>
</tr>
<tr>
<td>6–8 months</td>
<td>Observe the patient no less frequently than every third day and provide a maximum of three takeaway doses per week if stability has been demonstrated and contraindications are absent. Patients are to receive a maximum of two consecutive takeaway doses.</td>
<td>Observe the patient weekly and provide a prescription for one week of dispensed buprenorphine–naloxone if stability has been demonstrated and contraindications are absent.</td>
</tr>
<tr>
<td>8–12 months</td>
<td>Observe the patient no less frequently than every third day and provide a maximum of four takeaway doses per week if stability has been demonstrated and contraindications are absent. Patients are to receive a maximum of two consecutive takeaway doses.</td>
<td>Observe the patient fortnightly and provide a prescription for two weeks of dispensed buprenorphine–naloxone if stability has been demonstrated and contraindications are absent.</td>
</tr>
<tr>
<td>12–24 months</td>
<td>Patients should continue to be seen no less frequently than every fourth day and the maximum number of takeaway doses should remain at four per week. There may be some flexibility in how the takeaway doses are dispensed if stability has been demonstrated and contraindications are absent.</td>
<td>Patients may progress at 12 months to a 28-day prescription of dispensed buprenorphine–naloxone should they have been able to demonstrate stability on the fortnightly prescription and contraindications are absent.</td>
</tr>
</tbody>
</table>
6.6 Monitoring patients on takeaway doses

It is recommended that when the prescriber reviews a patient who has been receiving takeaway doses, the following issues should be dealt with by discussion and examination:

- acceptability of the dosing schedule, dose adequacy, side effects and other drug use
- sleep, mood and social functioning
- satisfaction with treatment
- mental state examination
- inspection of (at least) upper limbs for evidence of injection (groin and lower limb/neck sites should be inspected where suspicions or a history of injecting in these sites exist)
- observation for evidence of intoxication with other drugs
- urine drug screen.

6.7 When to stop providing takeaway doses

This is a difficult issue for a prescriber to deal with, as a patient receiving takeaway doses usually becomes distressed at any suggestion that this is to be curtailed. Often prescribers are unwilling to cause distress and conflict, so there is a powerful pressure to overlook signs of instability and continue prescribing takeaway doses. This is not good practice. It is common for drug-dependent patients to do well for a time, then relapse into periods of destructive drug use. For people in an opioid treatment program, this does not necessarily mean return to heroin use, but may involve developing an alcohol problem, or bingeing on stimulants or benzodiazepines. It is possible to intervene to reduce the risk of such destructive drug use. Supervised dosing is an important measure to reduce risk. Patients manifesting instability are not suitable for regular takeaway doses, and if a person on takeaway dosing develops an alcohol problem or other indicator of instability they need to be returned to supervised dosing.

A return to supervised dosing may be temporary, providing the patient with the opportunity to demonstrate that they have regained control — or, if a person relapses severely or repeatedly, it may be concluded that they are not able to deal with unsupervised treatment and need long-term supervised dosing.

Issues which dictate that a person should return to supervised dosing include:

- self report of relapse to heroin use, or to other dependent drug use
- credible evidence of diversion
- recent injection marks
- deterioration in psychological, physical or social wellbeing
- child-at-risk concerns, or DOCS involvement.

Takeaway doses should only be reintroduced gradually after at least four weeks of demonstrated stability.

6.8 Takeaway dosing and the dosing schedule

Takeaway doses should be the same as those consumed under supervision at the clinic or pharmacy.

Many patients change the timing of their dose when they receive takeaway doses. Patients on methadone may split their daily dose. Patients who were taking buprenorphine once every second day will often return to daily dosing, and some patients will prefer to split their dose into smaller doses twice or thrice daily rather than having a single morning dose. This is acceptable. However, patients should be advised to take the same total dose daily and not to vary their daily dose.

6.9 Takeaway doses and transfer to another prescribing doctor

Takeaway dose arrangements are not to be automatically transferred when patients are changing prescribing doctors. The new prescribing doctor is responsible for reassessing the patient’s suitability for takeaway doses and the appropriateness of the previous takeaway dose regimen. The new prescriber should communicate with the previous prescriber to obtain information that will assist in the assessment of the patient’s suitability for takeaway doses.

To adequately assess the patient’s stability and reliability, the number of takeaway doses provided by the new prescribing doctor during the first month should not exceed the number provided by the previous prescriber.

6.10 Authorisation, preparation, and supply of takeaway doses

Under current legislation, takeaway doses may be prepared only by a doctor or pharmacist, or under a pharmacist’s direct personal supervision.

The prescribing doctor is to provide the clinic or pharmacy with written authorisation (which should be in the prescriber’s own handwriting and signed) for takeaway doses. This must be attached to, or incorporated in, the current prescription and must specify the date or (when regular take-
away doses are provided) the days of the week on which the patient is to receive takeaway doses.

Each dose is to be supplied in a clean new container fitted with a child-resistant closure.

Individual takeaway doses should be labelled with:

- the name, strength and quantity of drug
- the patient's name in full
- original prescription (or identifying number)
- the date on which the takeaway dose was dispensed
- the date the takeaway dose is to be taken
- the required warning labels:
  - ‘KEEP OUT OF REACH OF CHILDREN’ in red on a white background
  - the driving hazard warning, preceded by an equilateral triangle coloured red: ‘THIS MEDICATION MAY CAUSE DROWSINESS AND MAY INCREASE THE EFFECTS OF ALCOHOL. IF AFFECTED DO NOT DRIVE A MOTOR VEHICLE OR OPERATE MACHINERY.’
- the name, address and phone number of the administration point.
- buprenorphine doses should remain in blister packaging and each dose should be individually labelled.

Takeaway doses are to be given to patients on the day before the scheduled absence from the dosing point. At that time the patient is to be told that methadone is for oral consumption only (or that buprenorphine–naloxone is for sublingual consumption only). The patient must be advised of the dangers of misusing the dose, the hazards of using it in combination with other drugs, and its toxic potential if taken by a child or anyone not tolerant of opioids.

6.11 Lost or stolen doses

Once in the possession of the patient, takeaway doses are the patient's responsibility. If a patient reports that takeaway doses have been lost, stolen or damaged, a replacement (either on-site or as a takeaway) should not be dispensed unless there is a medical indication to do so (such as to prevent withdrawal symptoms in pregnant patients).

If medically indicated, replacement doses should be carefully titrated against the observed clinical condition of the patient. Replacement doses are not usually full doses. Careful assessment and monitoring are required to ensure that the patient is not overdosed.

Regular loss of takeaway doses (for any reason) suggests that a return to on-site dosing is indicated.

6.11.1 Reporting lost doses

There is no legal requirement for any stolen/lost-dispensed methadone (or other substance listed in Schedule 8 of the Poisons List) to be reported to the police. There may of course be reasons why a report to the police is desirable.

Any loss or theft of a Schedule 8 substance, up to the point when it is dispensed (ie, from a clinic, pharmacy or hospital) must be reported to the Pharmaceutical Services Branch (PSB) of NSW Health (Ref Cl122 — Poisons and Therapeutic Goods Regulation 2002).

The PSB does not have to be notified of methadone being lost or stolen after it has been dispensed, but if it is notified, a note is made on the patient file.
### Specific clinical situations

#### Chapter summary

<table>
<thead>
<tr>
<th>Missed doses</th>
<th>See section</th>
</tr>
</thead>
<tbody>
<tr>
<td>When patients miss doses they may be tempted to use other drugs. If repeated doses are missed, tolerance to opioids may be reduced, increasing the risk of overdose when treatment is reintroduced.</td>
<td>7.1</td>
</tr>
<tr>
<td>Reintroducing methadone after missed doses:</td>
<td>7.1.1</td>
</tr>
<tr>
<td>- Assess patients for signs of intoxication and withdrawal.</td>
<td></td>
</tr>
<tr>
<td>- If the dose has not been collected for three or more consecutive days, withhold or reduce the dose until the prescriber has assessed the patient.</td>
<td></td>
</tr>
<tr>
<td>In general, if the patient has missed:</td>
<td>7.1.1</td>
</tr>
<tr>
<td>- One day: No change in dose.</td>
<td></td>
</tr>
<tr>
<td>- Two days: If no evidence of intoxication, administer normal dose.</td>
<td></td>
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<tr>
<td>- Three days: Administer half dose in discussion with the prescriber.</td>
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<tr>
<td>- Four days: Patient must see prescriber. Recomence at 40 mg or half dose, whichever is the lower.</td>
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<tr>
<td>- Five days or more: regard as a new induction.</td>
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</tr>
<tr>
<td>Reintroducing buprenorphine after missed doses for a patient on daily dosing:</td>
<td>7.1.2</td>
</tr>
<tr>
<td>- Assess patients for signs of intoxication and withdrawal.</td>
<td></td>
</tr>
<tr>
<td>- One or two daily doses missed and no contraindications: give a usual daily dose.</td>
<td></td>
</tr>
<tr>
<td>- Three or four daily doses missed, no contraindications and clear signs of withdrawal: give the usual daily dose up to 24 mg. Otherwise, give half to two-thirds of the usual daily dose.</td>
<td></td>
</tr>
<tr>
<td>- Five or more daily doses missed: treat patient as a new induction to treatment.</td>
<td></td>
</tr>
<tr>
<td>Reintroducing buprenorphine after missed doses for a patient on less frequent dosing:</td>
<td></td>
</tr>
<tr>
<td>- Assess patients for signs of intoxication and withdrawal.</td>
<td></td>
</tr>
<tr>
<td>- One or two doses missed and no contraindications: give a usual dose.</td>
<td></td>
</tr>
<tr>
<td>- Three or four doses missed, no contraindications and clear signs of withdrawal: give the usual daily dose (eg, half of the alternate day dose) up to 24 mg. Otherwise, give half to two-thirds of the usual daily dose.</td>
<td></td>
</tr>
<tr>
<td>- Five or more doses missed, or seven or more days without supervised dosing: treat patient as a new induction to treatment.</td>
<td></td>
</tr>
<tr>
<td>Vomited doses</td>
<td>7.2</td>
</tr>
<tr>
<td>Patients on methadone maintenance may vomit shortly after having their dose, which creates uncertainty about how much methadone has been absorbed.</td>
<td></td>
</tr>
<tr>
<td>Vomiting more than 20 minutes after methadone dose: Reassure patient that the dose will have been adequately absorbed.</td>
<td></td>
</tr>
<tr>
<td>Vomiting less than 20 minutes after methadone dose:</td>
<td></td>
</tr>
<tr>
<td>- If a patient who has been in treatment for more than two weeks has been observed by dispensing or clinical staff to vomit immediately after dosing, a half dose may be administered.</td>
<td></td>
</tr>
<tr>
<td>- If a patient is in the first two weeks of treatment or there is some uncertainty about the event, review the patient 4–6 hours after dosing. If at this time the patient appears to be experiencing withdrawal, a dose supplementation of up to half the patient's usual dose can be given.</td>
<td></td>
</tr>
<tr>
<td>Monitor pregnant patients who vomit their methadone dose closely and give a supplementary dose if necessary to avoid withdrawal, which distresses the fetus.</td>
<td></td>
</tr>
<tr>
<td>Buprenorphine doses are absorbed sublingually within 2–7 minutes. Vomiting after this time makes no difference to the absorbed dose.</td>
<td></td>
</tr>
</tbody>
</table>

#### Managing polydrug use

| Polydrug use | 7.3 |
| Polydrug use is common among opioid users. Many patients seeking methadone or buprenorphine treatment are likely to be dependent on benzodiazepines, alcohol or other drugs as well as opioids. Many are likely to be using other drugs at hazardous or harmful levels. |
Patients who present for dosing when intoxicated with alcohol or another central nervous system depressant should not be given their usual methadone/buprenorphine dose or a takeaway dose at that time.

Continued high-risk drug use is evidenced by frequent presentations when intoxicated, overdoses, chaotic drug using behaviour, and deteriorating medical or mental states due to drug use. Every effort should be made to therapeutically engage patients who continue polydrug use:

- Continue a courteous demeanour toward the patient, even when faced with difficult or confronting behaviour.
- Set clear boundaries around dosing, appropriate behaviour, and the expectations of participants in the treatment program. Provided that the prescriber considers it safe, an increase in dose, a change from buprenorphine to methadone, or a change in the frequency of dosing may be helpful.
- Invite patients to discuss concerns they may have about their recurrent intoxicated or debilitated presentation, and clearly convey the concerns that staff have regarding their risky drug use.
- Offer to support patients in other challenging or difficult areas of their life.
- Screen for specific circumstances (eg, living with other drug users) or conditions (eg, depression) that may be exacerbating hazardous or polydrug use.
- Consider possible coexisting mental health disorder (eg, anxiety, depression or paranoia) or organic cognitive impairment, and offer treatment or appropriate referral when indicated.
- Provide patients with documentation of concerns and suggested or agreed solutions.
- Wherever possible, invite patients into a collaborative discussion before notifying them of significant treatment changes.
- A motivational interviewing approach may work for patients who are unsure whether they wish to change their polydrug use.
- If possible, document an action plan in collaboration with the patient for reducing polydrug use.

Weigh the risks of combining methadone or buprenorphine with other drug use against the benefits in reducing harms, improving health and improving social functioning. If the disadvantages predominate, and the patient appears unwilling or unable to change, it may be necessary to arrange the patient’s gradual withdrawal from treatment.

Patients who are currently using other opioids, benzodiazepines or alcohol in large doses should not have takeaway doses and should generally be dosed at clinics, not at pharmacies.

Prescribing benzodiazepines to patients who are dependent on benzodiazepines as well as opioids may be necessary, but caution must be exercised. Patients with benzodiazepine dependence frequently acquire prescriptions from multiple sources: register with the Health Insurance Commission’s Prescription Shopping Information Service, and try to verify the patient’s history of obtaining benzodiazepines before prescribing.

The goal of treatment is safe withdrawal from benzodiazepines, not patient comfort. Diazepam should be the only benzodiazepine prescribed, all doses should be administered under supervision as a single daily dose, and while receiving benzodiazepines patients should not receive takeaway doses of methadone. Never initiate benzodiazepine treatment at the same time as methadone maintenance, as this is the period in which risk of overdose is greatest.

Patients in an opioid treatment program may require assistance to withdraw from other drugs while continuing methadone or buprenorphine treatment. This “selective detoxification” should usually be managed by the patient’s prescriber. The NSW Health clinical practice guidelines for the management of withdrawal will be of assistance. Drug and alcohol medical specialists should be consulted in more complicated cases.

Overdose

Naloxone (Narcan) given intravenously, intramuscularly or subcutaneously is the treatment of choice for an opioid overdose, since it leads to immediate reversal of the overdose. Admission to hospital should always be recommended, as the effect of naloxone does not last as long as the effect of heroin or methadone.
### Methadone overdose:
- Naloxone should be given as a prolonged infusion when treating methadone overdose. Patients who are thought to have taken a methadone overdose require prolonged observation.
- Methadone overdose is usually associated with use of other drugs and usually occurs within the first few days of induction to treatment. Patients should be warned of these risks.
- Deaths often occur at home during sleep. Dosing in the morning reduces this risk. Family members should be warned that deep snoring during induction to treatment could be a sign of dangerous respiratory depression and should be reported to the prescriber.

### Buprenorphine overdose:
- The risk of lethal overdose on buprenorphine in an opioid-tolerant individual is less than that associated with methadone.
- However, the effects of buprenorphine are not reversed by the usual doses of naloxone. Doses of 10–35 mg/70 kg (10–30 times the dose used to reverse heroin overdose) may be required to reverse the effects of buprenorphine toxicity.
- Consider the long duration of action of buprenorphine when treating the effects of an overdose.

### Incorrect dosing

#### Incorrect methadone (over) dose administered:
- If the overdose is less than 50% of the usual dose, the dispenser can warn the patient about risks of extra drug use, risks of driving or using machinery, signs and symptoms of overdose and advise him or her to go to a hospital emergency department if any symptoms develop. The dispenser must advise the prescriber of the dosing error and record the event.
- If the overdose is more than 50% of the usual dose, the dispenser should contact the prescriber and drug and alcohol medical specialist immediately. If the prescriber or drug and alcohol specialist decides that the patient requires hospitalisation, he or she should be accompanied to the hospital to ensure admitting staff receive clear information on the circumstances. If the patient has left before the mistake is realised, every attempt must be made to contact him or her.
- Patients in the first 2 weeks of treatment who receive an overdose of any size require observation for 4 hours (longer if signs of intoxication develop).
- Patients who have been on a dose > 40 mg/day consistently for two months will generally tolerate a single double dose without significant symptoms. For a dose greater than double the usual daily dose, the patient will require observation for at least 4 hours (longer if signs of intoxication develop).
- Patients in whom the level of tolerance is uncertain (dose less than 40 mg/day, or in treatment for less than 2 months, or receiving takeaway doses) require observation for at least 4 hours if they are given a dose 50% higher than their usual dose (longer if signs of intoxication develop).

#### Incorrect buprenorphine (over) dose administered:
- Warn the patient of possible effects, risks associated with extra drug use, and against driving or operating machinery.
- Monitor the patient for at least six hours if the patient is showing signs of toxicity or has commenced treatment in the last 2 weeks, the dose administered is 16 mg or more, given to a patient whose normal dose is 4 mg or less, or a dose 64 mg or more was administered.
- The prescriber should review the patient before the next dose.

### High dose treatment

- There is no systematic evidence to support the greater efficacy of methadone doses above 150 mg. Split dosing is more effective than higher dosing in patients who are rapid methadone metabolisers. A second opinion is recommended when considering high dose treatment.

- There is no evidence for the greater efficacy of buprenorphine doses above 16 mg. Higher doses are expensive and bring problems of diversion.
Managing difficult behaviour

The Treatment Agreement signed by all patients states:

“The following actions will be taken sequentially when clients do not comply with conditions of the program:

1. A formal warning will be given.
2. A change in conditions of program will occur including removal of takeaway doses and the requirement to attend more frequent appointments.
3. Transfer to a more supervised treatment setting.
4. Withdrawal from the program.

Certain actions, namely violence or threat of violence against staff or other patients, property damage or theft from the methadone/buprenorphine program, drug dealing on or near treatment premises, and repeated diversion of methadone/buprenorphine may warrant immediate discharge from treatment.”

When confronted with challenging behaviour, staff should remain calm, listen to the individual’s concerns in an empathic, non-confronting manner, emphasise their desire to help, and try to make the individual more comfortable.

Treating inpatients

In general, methadone or buprenorphine treatment should continue in hospital. The hospital medical officer managing the patient should consult with the prescriber.

Buprenorphine binds strongly with opioid receptors and there is a theoretical risk that it may interfere with the effectiveness of other opioids prescribed for pain relief.

A missed dose is not a medical emergency and it is generally not appropriate to prescribe methadone or buprenorphine in the emergency department.

Patients who have takeaway doses for the days they are in hospital should be requested to hand the takeaway doses to the ward staff and have their methadone or buprenorphine dispensed through the hospital pharmacy.

Patients on methadone or buprenorphine treatment who are experiencing acute pain in hospital often have their pain undertreated. Because of their tolerance of opioids, they may require larger doses of analgesia for adequate pain relief, but the initial dose and route of administration should be that normally prescribed.

When a prescriber or a staff member at a dosing location is contacted regarding inpatient treatment of a person receiving methadone or buprenorphine, they should provide all possible assistance to the hospital medical officer (information about the legal requirements for prescribing opioid treatment, patient history, and the significance of the patient’s current dosing regimen).

The senior registered nurse or pharmacist at the dosing location should document that the patient has become an inpatient and is being dosed elsewhere. To avoid double dosing, he/she should confirm that the patient has been discharged and confirm the date on which the patient last received a dose before recommencing dosing. When a prescriber is contacted regarding treatment, he/she must ensure that the dosing location has been notified.

Opioid dependent people who are not in an opioid treatment program may experience withdrawal if admitted to hospital. Methadone or buprenorphine may be used to treat withdrawal symptoms if withdrawal symptoms could reasonably be expected to interfere with the optimum medical management of the patient, or if the patient is suffering from a serious or life-threatening illness and the patient’s premature self-discharge before completion of therapy would prejudice optimum management.

Patients requiring pain relief in the primary care setting

Opioids should not be prescribed to opioid dependent people outside a regulated opioid treatment program except in rare instances (eg, to treat severe pain of trauma or other medical emergency).

Patients receiving methadone or buprenorphine treatment who require acute pain relief can be managed as for patients who are not opioid dependent, although doses of analgesic drugs may need to be higher.

Some patients with chronic pain develop opioid dependence and may be appropriately treated by admission to an opioid treatment program.

Patients on methadone or buprenorphine treatment who experience chronic pain may require specialist management.
Pregnancy and breastfeeding

- Pregnant women who use opioid drugs such as heroin are at an increased risk of developing serious complications in pregnancy.
- Newborn from these pregnancies are at risk of neonatal abstinence syndrome and sudden infant death syndrome.
- Opioid withdrawal during pregnancy carries particular risks and requires specialist care.
- Opioid treatment during pregnancy:
  - helps stabilise drug use and lifestyle
  - reduces or eliminates illicit opioid drug use and can help stabilise the in utero environment
  - facilitates access to comprehensive antenatal and postnatal care
  - does not increase the risk of congenital abnormalities in the fetus.

Buprenorphine is not recommended for pregnant women and breastfeeding women at present because evidence for its safety is limited.

Methadone maintenance in pregnancy:
- Pregnant women should be maintained on an adequate dose of methadone to achieve stability and prevent relapse or continued illicit opioid drug use. Women already in methadone treatment who become pregnant can continue in treatment.
- The bioavailability of methadone is decreased in the later stages of pregnancy. It may be necessary to divide the daily dose and possibly to increase the dose in the third trimester of pregnancy to avoid withdrawal symptoms and minimise additional drug use.
- Antenatal and postnatal care should be managed in collaboration with a specialist obstetric service experienced in the management of drug dependency during pregnancy.
- Dose reductions or withdrawal, if requested by the patient, are best carried out in the second trimester of pregnancy.
- Breastfeeding should be encouraged.

Neonatal withdrawal

- All babies born to opioid dependent mothers should be observed by experienced staff for the development of withdrawal signs.
- Supportive treatment of neonatal withdrawal involves minimising environmental stimuli and enhancing the baby's comfort. Treatment with morphine should be considered for infants who exhibit severe signs of withdrawal, but morphine may depress respiration and should be used with extreme caution. It is recommended that neonatal care be managed in collaboration with a specialist obstetric or paediatric service experienced in the management of babies born to drug dependent mothers.

Child protection

- On initial assessment, at treatment review and when assessing eligibility for takeaway doses, it is important to consider the safety and welfare and wellbeing of any children within the patient's care.
- Health care workers have a duty under the Children and Young Persons (Care and Protection) Act 1998 (NSW) to notify the Department of Community Services (DOCS) whenever they suspect that a child or young person may be at risk of harm through abuse or neglect. When necessary, this duty overrides the duty to maintain patient confidentiality.
- A parent's enrolment in an opioid treatment program is not itself a reason to make a report to DOCS.
- In relation to newborn children of opioid dependent mothers, a multidisciplinary case conference should be convened in accordance with the NSW Health neonatal abstinence syndrome guidelines (2005) to formulate a discharge plan for mother and baby.
Inadvertent consumption of methadone by a child

- This is a potentially life-threatening situation.
- Assess the level of consciousness and monitor this continuously until the child is in the care of ambulance or other qualified staff.
- Refer the child to a hospital emergency department without delay, providing the information available about the amount taken and the time.
- Administer oxygen if available.
- Consider naloxone administration if the child is obtunded. Document any treatment given.
- Notify the prescriber of the takeaway dose and advise the NSW Department of Health of the incident.
- Consider notifying other authorities depending on circumstances:
  - A report to DOCS should be made (see section 7.14, Child protection, on page 76).
  - Police may be involved in exceptional circumstances.

Domestic violence

Prescribers should be alert to the possibility of domestic violence and routinely screen all female patients for risk (see Appendix H, page 128) and make them aware of services to assist.

Patients with coexisting mental health problems

- The prevalence of mental health problems is higher among opioid users than in the general population.
- Assessing mental health status should be an integral part of the care of patients in an opioid treatment program. Checking for suicidal thoughts should be routine.
- Methadone or buprenorphine maintenance can reduce levels of psychiatric distress, with improvement apparent within weeks of commencement of treatment. Screen mental health status again after stabilisation on treatment.
- Psychotherapy as an adjunct to methadone or buprenorphine treatment may benefit patients with medium and high levels of psychiatric problems.
- Evidence of the effectiveness of antidepressants as adjuncts to methadone or buprenorphine treatment is equivocal. Tricyclic antidepressants have been associated with an increased risk of overdose; so selective serotonin reuptake inhibitors are preferred.

Patients with HIV

- Both methadone and buprenorphine have interactions with HIV medications.

Patients with hepatitis B or C

- Refer patients who are acutely infected or who are chronic carriers of hepatitis B to a gastroenterologist for specialist assessment and follow-up.
- Recommend hepatitis B vaccinations to all patients who are found to have no immunity to the hepatitis B virus.
- A high percentage of patients entering the Opioid Treatment Program will be hepatitis C antibody positive. They should be treated in accordance with Hepatitis C, a management guide for general practitioners.
- Abrupt changes in liver function might necessitate substantial dose adjustments.

Dosing arrangements for severely ill patients

- Some patients may become temporarily or permanently unable to attend their usual dosing location. Options include:
  - using another dosing location that may be closer to the patient or provide easier access
  - takeaway doses
  - collection of doses by a responsible carer
  - dosing at home.
Multiple dosing locations

- For practical reasons, patients may receive methadone or buprenorphine from more than one dosing location, but care must be taken to avoid missed or duplicated dosing. One site is nominated as the primary dosing site and is responsible for ensuring that the patient is dosed appropriately. Regular communication should occur between both dosing locations to ensure safety and monitor the patient's progress.

Justice Health settings

- Patients who are in an opioid treatment program when they enter prison or a juvenile detention centre should have their treatment continued until reviewed by the Justice Health Service.
- Other inmates may begin methadone or buprenorphine treatment while in prison or a juvenile detention centre. The indications for treatment are the same for inmates as for the general population.
- The transition from detention to the community involves a risk that the released inmate will return to illicit opioid use. Released inmates should have access to public dosing and case management in their local Area Health Service.

Patients under legal supervision

- Public and private opioid treatment services are responsible for dosing any of their patients who are being held in police custody, except for patients held in cells where Corrections Health nurses are available to do the dosing. The police should inform the relevant service provider as early in the day as possible that a patient will require a dose of methadone.
- For dosing in cells, the patient's regular methadone/buprenorphine provider should provide documentation of:
  - patient identification, including photograph and/or physical description
  - a copy of the prescription/treatment chart for the patient
  - verification of the time and date of the administration of the patient's last dose
  - verification of the number of takeaway doses (if any) provided when the patient was last seen for dosing.

Urgent prescriptions due to unforeseen circumstances

- In special circumstances, a patient may require a prescription or an authorisation to receive a dose at a location other than their usual dosing site. If the patient's regular prescriber cannot be contacted, a locum prescriber can be requested to provide a prescription to cover the special circumstances. If no details can be obtained about an individual claiming to be on methadone or buprenorphine from a prescriber or a dispensing site (public or private) then it is appropriate to refuse to prescribe or provide these drugs.

Arrangements for travel

- The transfer of a patient's methadone or buprenorphine treatment within NSW, between states and overseas should be carried out by the prescriber.
- The PSB need not be notified of temporary changes of dosing location.
- If overseas travel requires the patient to carry takeaway doses, the prescriber should clarify with the consulates of the intended destinations their position on a foreigner entering in possession of methadone or buprenorphine. Providing a letter stating that the person is in possession of the drug to treat a medical condition in accordance with Australian laws is usually adequate.
7.1 Missed doses

A review of fatalities associated with methadone treatment suggested that patients who missed three or more consecutive doses were at risk of overdose. Presumably, this reflected a degree of reversal of neuroadaptation, and possibly the use of other sedative drugs. Therefore, when a patient misses three or more doses they need to be reviewed by an experienced clinician before resuming treatment. As in all situations, where patients are intoxicated, no methadone should be administered. The circumstances surrounding missing doses should be documented.

7.1.1 Reintroducing methadone after missed doses

When patients are not intoxicated on presentation, one recommended procedure is:

<table>
<thead>
<tr>
<th>Missed 1 methadone dose:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Provide usual dose.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Missed 2 consecutive doses:</th>
</tr>
</thead>
<tbody>
<tr>
<td>If dose &gt; 80 mg, administer half usual dose.</td>
</tr>
<tr>
<td>If dose 40–80 mg, administer 40 mg.</td>
</tr>
<tr>
<td>If dose &lt; 40 mg, administer usual dose.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Missed 3–5 consecutive doses:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Review by experienced clinician, and:</td>
</tr>
<tr>
<td>■ investigate why doses were missed</td>
</tr>
<tr>
<td>■ take history of drug use over preceding three days</td>
</tr>
<tr>
<td>■ monitor for signs of intoxication and withdrawal</td>
</tr>
<tr>
<td>■ if not intoxicated, administer half usual dose or 40 mg, whichever is lower.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Missed &gt; 5 doses:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treat as a new induction to treatment.</td>
</tr>
</tbody>
</table>

7.1.2 Reintroducing buprenorphine after missed doses

Missed doses are a common problem with buprenorphine, as its long duration of action means many patients attend erratically, without experiencing much withdrawal discomfort. However, this tends to result in suboptimal dosing, and should be discouraged. Patients who regularly miss days in treatment and continue frequent heroin use may be better managed by transfer to methadone.

<table>
<thead>
<tr>
<th>Missed 1–2 buprenorphine doses:</th>
</tr>
</thead>
<tbody>
<tr>
<td>■ Ask how patient is — record symptoms of withdrawal, any drug use since last dose.</td>
</tr>
<tr>
<td>■ Record why dose was missed and address access issues if they are likely to reoccur.</td>
</tr>
<tr>
<td>■ Assess state of opioid intoxication or withdrawal and record.</td>
</tr>
<tr>
<td>■ If patient has no contraindications to receiving buprenorphine then dose with the existing daily dose.</td>
</tr>
<tr>
<td>■ If the patient reports opioid use in the last 12 hours or is exhibiting signs of intoxication with opioids, withhold dose and ask the patient to present again in 2–4 hours.</td>
</tr>
<tr>
<td>■ If the dispensing staff are unsure, seek a medical review.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Missed 3–4 consecutive doses:</th>
</tr>
</thead>
<tbody>
<tr>
<td>■ Ask how patient is — record symptoms of withdrawal, any drug use since last dose.</td>
</tr>
<tr>
<td>■ Record why dose was missed and address access issues if they are likely to reoccur.</td>
</tr>
<tr>
<td>■ Assess state of opioid intoxication or withdrawal and record.</td>
</tr>
<tr>
<td>■ If the patient reports opioid use in the last 12 hours or is exhibiting signs of intoxication with opioids, withhold dose and ask the patient to present again in 2–4 hours.</td>
</tr>
<tr>
<td>■ If the patient is exhibiting signs of withdrawal and there are no contraindications to receiving a dose of buprenorphine, then they should be dosed as follows:</td>
</tr>
<tr>
<td>◆ For daily doses of 8 mg or below: give the usual daily dose.</td>
</tr>
<tr>
<td>◆ For daily doses of 8–24 mg, when the patient is exhibiting clear withdrawal: given the usual daily dose.</td>
</tr>
<tr>
<td>◆ For daily doses of 8–24 mg, when withdrawal is less apparent: give half to two-thirds of the usual daily dose.</td>
</tr>
<tr>
<td>◆ For daily doses above 24 mg: give half to two-thirds of the usual daily dose.</td>
</tr>
<tr>
<td>■ The following day, as long as there have been no problems, return to the usual daily dose.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Missed &gt; 5 doses:</th>
</tr>
</thead>
<tbody>
<tr>
<td>■ As for methadone, the patient should be reviewed by the prescriber and reasons for non-attendance should be explored. Discuss how best to facilitate successful re-entry into treatment.</td>
</tr>
<tr>
<td>■ Treat as a new induction to treatment.</td>
</tr>
</tbody>
</table>
7.1.2.2 Procedure for patients receiving less frequent dosing

Missed 1–2 buprenorphine doses:
- Ask how patient is — record symptoms of withdrawal, any drug use since last dose.
- Record why dose was missed and address access issues if they are likely to reoccur.
- Assess state of opioid intoxication or withdrawal and record.
- If patient has no contraindications to receiving buprenorphine then dose with the existing daily dose.
- If the patient reports opioid use in the last 12 hours or is exhibiting signs of intoxication with opioids, withhold dose and ask the patient to present again in 2–4 hours.
- If the dispensing staff are unsure, seek a medical review.

Missed 3–4 consecutive doses:
- Ask how patient is — record symptoms of withdrawal, any drug use since last dose.
- Record why dose was missed and address access issues if they are likely to reoccur.
- Assess state of opioid intoxication or withdrawal and record.
- If the patient reports use of heroin in the last 6–8 hours or is exhibiting signs of intoxication with opioids, withhold dose and ask the patient to present again in 2–4 hours.
- If the patient is exhibiting signs of withdrawal and there are no contraindications to receiving a dose of buprenorphine then they should be given the usual daily dose (eg, half of the alternate day dose), up to a limit of 24 mg.
- The following day, as long as there have been no problems, the patient may be return to the usual dosing schedule.

Missed > 5 doses, or no supervised dose for more than seven days:
- As for methadone, the patient should be reviewed by the prescriber and reasons for non-attendance should be explored. Discuss how best to facilitate successful re-entry into treatment. In rural areas, the patient should be assessed by the prescriber or provide information by a detailed telephone discussion.
- Treat as a new induction to treatment.

7.2 Vomited doses

Occasionally patients find that methadone causes nausea and vomiting. This situation is aggravated in pregnancy but non-pregnant patients also suffer from the complication on occasions. Some patients find that switching from one preparation of methadone to the other can reduce this side effect. Although the pharmacology of this is not understood, the alternative methadone solution should be offered to patients if vomiting is an issue.

In patients suffering regularly from vomiting after a dose, consideration should be given to administering the dose slowly at the dispensing point, if this is possible, or moving to a split-dosing regimen. Patients who have takeaway doses should be advised to sip the dose slowly to reduce gastric irritation.

As vomiting does not necessarily result in the expulsion of the entire gastric contents, some or even most of the dose may be absorbed. The time elapsed is also significant: it takes 20–30 minutes for the entire dose to be absorbed.

7.2.1 Vomiting later than 20 minutes after consumption of methadone dose

Reassure the patient that the dose will have been adequately absorbed and provide relevant assistance or advice in relation to the gastrointestinal problems he or she is experiencing.

7.2.2 Vomiting within 20 minutes of consumption of methadone dose

Uncertainty regarding the amount of methadone absorbed dictates that no extra methadone be given without review of the patient by an experienced clinician.

If a patient who has been in treatment for more than two weeks has been observed by dispensing or clinical staff to vomit immediately after dosing, a half dose may be administered. A prescription needs to be written for the extra dose.

When a patient is in the induction phase (the first two weeks of treatment) or there is some uncertainty about the event, review the patient 4–6 hours after consumption of the dose when plasma levels will be at their peak. If at this time the patient appears to be experiencing withdrawal, a dose supplementation of up to half the patient’s usual methadone dose can be given.

7.2.3 Pregnant patients who vomit a dose

Withdrawal symptoms can produce fetal distress, and special efforts should be made to monitor the progress of pregnant patients who have vomited their dose. Pregnant patients should receive treatment as for non-pregnant patients (see sections 7.2.1 and 7.2.2 on page 63), but every effort should be made to review the patient at 4–6 hours (in person or by
phone if direct observation cannot be arranged) to ensure that no signs of withdrawal are developing. If dosing appears to have been inadequate then a further smaller dose may be considered.

7.2.4 Vomiting a buprenorphine dose

Buprenorphine is absorbed sublingually within 2–7 minutes. Vomiting after this time makes no difference to the absorbed dose.

7.3 Managing polydrug use

Polydrug use is common among opioid users. Many patients seeking methadone or buprenorphine treatment are likely to be dependent on benzodiazepines, alcohol or other drugs as well as opioids. Many are likely to be using other drugs at hazardous or harmful levels.

The use of other drugs, particularly sedatives (such as alcohol and/or benzodiazepines) in combination with opioids, significantly increases the risk of respiratory depression and death. In Australia, more than 90% of deaths during stabilisation on methadone involve other drugs, in particular alcohol, benzodiazepines and antidepressants. Additional drug use during the early stages of methadone or buprenorphine maintenance is common. Although this creates safety issues, it will usually be in the patient’s interest to persist with treatment. The risk arising from other drug use (e.g., overdose, serious illness, social deterioration) should be balanced against the potential risk of increased hazardous drug use if treatment is withdrawn.

Patients at risk from polydrug use:
- frequently present intoxicated or with signs of benzodiazepine or alcohol withdrawal
- regularly use other drugs at levels above the normal therapeutic dose.

Specialist advice should be sought when treating patients at high risk from polydrug use.

The use of drugs other than prescribed methadone or buprenorphine (including alcohol and tobacco) may be monitored by self-report, by regular urine tests for drugs or by observation of changes in the patient’s clinical condition or behaviour. If there is a strong therapeutic relationship, patients may report problematic use of other drugs. Patients using other drugs should be provided with interventions that are based, wherever possible, on evidence of effectiveness, and which take into account patient wishes.

The relative paucity of research and evidence on effective interventions for patients who use several drugs contributes to considerable variance of clinician opinion on how best to manage this complex problem. Best practice requires a firm approach to the setting and supervision of dosing, while continuing to show a professional and courteous demeanour towards the patient.

7.3.1 Intoxicated presentation

Patients exhibiting signs of intoxication should not be dosed.

Patient safety is the key consideration in responding to those who present for dosing while intoxicated with opioids, alcohol or other drugs.

Patients should always be assessed by the nurse or pharmacist administering the dose before the dose is given. Patients who appear intoxicated with alcohol or another central nervous system (CNS) depressant should not be given their usual methadone/buprenorphine dose or a takeaway dose at that time. They should be asked to return later when they are no longer intoxicated.

If intoxication is evident but appears mild, the patient may be given a reduced dose — but only after being reviewed by the prescriber.

For symptoms and signs of drug intoxication, see Appendix I (page 132).

7.3.2 Continued high risk drug use

Continued high-risk drug use is evidenced by:
- frequent presentations when intoxicated
- overdoses
- chaotic drug using behaviour
- deteriorating medical or mental state due to drug use.

Continued drug use can affect patient stability and treatment progress and place the patient at risk of:
- relationship, social and employment problems
- contracting infectious diseases
- involvement in crime.

Every effort should be made to therapeutically engage those patients who continue polydrug use. Although the evidence about effective engagement with this group of patients is limited, recommended practice includes:
- Continuing a courteous demeanour toward the patient, even when faced with difficult or confronting behaviour.
- Setting clear boundaries around dosing, appropriate behaviour, and the expectations of participants in the treatment program. Provided that the prescriber considers it safe, an increase in dose, a change from buprenorphine to methadone or a change in the frequency of dosing may be helpful.
- Inviting patients to discuss concerns they may have about their recurrent intoxicated or debilitated presentation,
and clearly conveying the concerns that staff have regarding their drug use.

- Offering to support patients in other challenging or difficult areas of their life.

- Screening for specific circumstances (eg, living with other drug users) or conditions (eg, depression) that may be exacerbating hazardous or polydrug use.

- Considering the possibility of coexisting mental health disorder (anxiety, depression or paranoia) or organic cognitive impairment, and offering treatment or appropriate referral when indicated.

- Providing patients with documentation of concerns and suggested or agreed solutions. This should include an agreement between patient and clinician on objectives to reduce drug use, consequences for treatment if hazardous polydrug use continues, and a review date. Such a written summary becomes particularly relevant if — because of intoxication or memory impairment — the patient may not recall the meeting at a later time.

Wherever possible, invite patients into a collaborative discussion before notifying them of significant treatment changes. Although patients may be unhappy with treatment changes required by continuing polydrug use (eg, loss of takeaway doses or a change in dosing location), a frank but courteous discussion can help them accept the decision and provide valuable feedback about their presentation.

A motivational interviewing approach may work for patients who are unsure whether they wish to change their polydrug use.

Further information on motivational interviewing

An action plan resulting from a meeting with a patient who wishes you and your service to work with them to change their concurrent drug-using behaviour might include:

- assistance with selective detoxification (inpatient or outpatient)
- strategies to cope with withdrawal of the other drugs
- relapse prevention training
- other skills that will assist with reduction, or abstinence from, other drug use (eg, relaxation techniques, social skills training)
- alterations to methadone or buprenorphine dose
- an agreement on treatment objectives and incentives (eg, offering a regular takeaway dose after one month’s abstinence from alcohol)

- an agreement on how frequently progress will be monitored.

Clearly document this plan in the patient’s clinical record, and wherever possible, provide patients with their own copy.

Frequently review the disadvantages versus the benefits of methadone or buprenorphine treatment. Weigh the risks of combining methadone or buprenorphine with other drug use against the benefits in reducing harms, improving health and improving social functioning. If the disadvantages predominate, and the patient appears unwilling or unable to change, it may be necessary to arrange the patient’s gradual withdrawal from the opioid treatment program. In such cases, contingency plans for management of withdrawal or re-engagement in treatment should be provided.

Patients who are currently using other opioids, benzodiazepines, amphetamines or alcohol in large doses should not have takeaway doses and should generally be dosed at clinics, not at pharmacies.

7.3.3 Benzodiazepines

Up to 35% of people in an opioid treatment program take benzodiazepines regularly or intermittently; these patients tend to do very poorly. There are no clear therapeutic indications for long-term benzodiazepine prescribing, and an important objective of methadone treatment should be to minimise use of benzodiazepines by patients.

Benzodiazepines are not safe drugs when taken in conjunction with opioids, particularly methadone. A recent Melbourne study of adolescents who had died of drug overdose found a pattern of escalating attendance at doctors’ surgeries in the six months before death, the main reason for attending being to obtain prescriptions. Most cases of fatal opioid overdose involve the concomitant use of benzodiazepines.

Patients are often highly skilled at obtaining prescriptions, and present a range of plausible and compelling reasons why they should receive benzodiazepines — of which the most common is that they are benzodiazepine dependent, and at risk of seizures if not prescribed benzodiazepines.

In seeking to manage these patients, there is a trade-off between the risks of trying to stabilise the patient by prescribing benzodiazepines (thereby placing patients at risk of overdose, prolonging the problem, and adding to the pool of black market drugs) or not intervening and placing the patient at risk of major withdrawal.

It is probably safer not to prescribe benzodiazepines at all to patients on methadone. If a prescriber is persuaded that it may be in the patient’s interests to manage benzodiazepine dependence by prescribing reducing doses of a benzodiazepine, several critical steps must be taken (and documented):
Obtain a careful history of benzodiazepine use, accepting that overestimation is common. In assessing tolerance, many users will report levels of use associated with intoxication and sedation. This is far in excess of what is required to avoid withdrawal.

Endeavour to find corroborative evidence of major withdrawal in the past (e.g., hospital admissions with seizures) rather than accepting the history.

Collect a urine test to confirm benzodiazepine use.

Register with the Health Insurance Commission’s Prescription Shopping Information Service, and try to verify the patient’s history of obtaining benzodiazepines before prescribing. If prescribing, it must be on the understanding that the patient will not obtain scripts from other prescribers, and this should be periodically checked with the HIC.

Define the goals of treatment — namely, to withdraw safely from benzodiazepines. The issue is safety, not patient comfort. Diazepam should be the only benzodiazepine prescribed, all doses should be administered under supervision as a single daily dose, and while receiving benzodiazepines patients should not receive takeaway doses of methadone. Never initiate benzodiazepine treatment at the same time as methadone maintenance, as this is the period in which risk of overdose is greatest.

If patients stabilise on a dose in the range 40–80 mg of diazepam daily, withdrawal should be at the rate of at least 5 mg per week until the dose reaches 40 mg, then 2.5 mg/week. At this rate, reducing from 80 mg diazepam will take nearly six months. A maximal rate of withdrawal would be to reduce the dose by 10 mg at weekly intervals until 40 mg, then by 5 mg at weekly intervals. Withdrawal will still take 12 weeks.

During withdrawal, patients should be monitored with clinical reviews and by checking the Doctor Shopping Information Service. The experience of most clinicians is that few patients comply with treatment, and most continue to seek and obtain additional benzodiazepines. In this situation, there is no point continuing with a “withdrawal” treatment; the treatment simply becomes part of the source of benzodiazepines.

Unless the patient requires admission to a hospital for detoxification, the patient’s prescriber should take responsibility for coordinating selective detoxification.

The prescriber should:

- review the patient frequently
- monitor the patient closely for evidence of intoxication with sedative drugs in combination with methadone or buprenorphine
- provide only small quantities of withdrawal medication at a time (preferably daily pick-up of withdrawal medication).

Usually the prescriber will personally manage the withdrawal. If this is not practical, the prescriber should work with a medical practitioner in managing selective detoxification.

Prescribers should document withdrawal protocols to be followed for patients undergoing selective detoxification, including medication regimens, clinical monitoring requirements, identification and management of intoxication and provision of psychosocial support. The NSW Health clinical practice guidelines for the management of withdrawal (2006) will be of assistance. Drug and alcohol medical specialists should be consulted in more complicated cases, or if the prescriber is unfamiliar with the accepted treatment approach.

### 7.4 Overdose

The use of benzodiazepines, illicit opioids and alcohol in combination with methadone or buprenorphine can result in toxicity and life-threatening overdose. In addition, toxicity from the combination of drugs can place patients at risk of injury and other health and social problems.

The mu receptor opioid antagonist naloxone (Narcan) given intravenously, intramuscularly or subcutaneously is the treatment of choice for opioid overdose, since it leads to immediate reversal of the overdose. Gaining intravenous access may be problematic in some long-term injectors in which case it may be quicker to give naloxone (0.8–1.6 mg) subcutaneously or intramuscularly. This has the advantage of bringing the patient around slightly more gently than an intravenous bolus, which can produce abrupt and very uncomfortable withdrawal. Admission to hospital should always be recommended. The plasma half-life of naloxone is 1–2 hours and the duration of effect from a single intravenous dose is as short as 45 minutes, compared to 4–6 hours for the physiological effects of heroin and 24–36 hours for methadone.

All clinics need to have planned procedures for managing an overdose. The response to an overdose will depend upon the severity and urgency of the situation but should, if necessary,
include cardiopulmonary resuscitation, calling for an ambulance (or the resuscitation team if associated with a hospital), calling for urgent medical assistance, closely monitoring the patient and (if indicated and possible) administering oxygen.

7.4.1 Methadone

In Australia, more than 90% of deaths during stabilisation on methadone involve other drugs, in particular, alcohol, benzodiazepines and antidepressants. Warn patients of the risks associated with using other drugs with methadone. Typically, overdose occurs around the third or fourth day of methadone induction. Deaths often occur at home during sleep, many hours after blood methadone concentrations have peaked.

To reduce this risk, administer methadone in the morning so that methadone concentrations peak when patients are normally awake and other people may be around if overdose should occur.

Patients who are thought to have taken a methadone overdose require prolonged observation. Family members should be warned that deep snoring during induction to treatment could be a sign of dangerous respiratory depression and should be reported to the prescriber. Heavy snoring during maintenance treatment may be associated with sleep apnoea and should also be reported.

Because of the long plasma half-life of methadone, naloxone should be given as a prolonged infusion when treating methadone overdose.

7.4.2 Buprenorphine

The risk of lethal overdose on buprenorphine in an opioid-tolerant individual is less than that associated with the use of other opioid medications, such as methadone.

However, the effects of buprenorphine, due to its strong affinity to \( \mu \) opioid receptors, are not reversed by the usual doses of the opioid antagonist, naloxone. Doses of 10–35 mg/70 kg (10–30 times the dose used to reverse heroin overdose) may be required to reverse the effects of buprenorphine toxicity.

The long duration of action of buprenorphine should be taken into consideration when determining the length of treatment needed to reverse the effects of an overdose.

7.5 Incorrect dose administered

In the event of an accidental overdose, the critical issues that determine how clinicians should respond are the patient’s level of tolerance and the amount of medication given in error.

7.5.1 Preventing incorrect doses

- Establish procedures for easy and accurate identification of patients.
- Identify on treatment cards those patients who are being stabilised.
- Identify on treatment cards those patients with similar names.
- Ensure patients are informed of the risks, signs and symptoms of overdose.

7.5.2 Incorrect dose higher than the prescribed dose

7.5.2.1 Methadone

A patient who receives a methadone dose in excess of that prescribed is at risk of overdose. The dispenser should follow the following procedures:

**Overdose up to 50% of the normal dose:**

- Advise the patient of the mistake and carefully explain the possible consequences.
- Warn the patient of the risks associated with extra drug use, and warn against driving or operating machinery.
- Inform the patient about signs and symptoms of overdose and advise him or her to go to a hospital emergency department if any symptoms develop.

### Signs and symptoms of methadone overdose

- Pinpoint pupils
- Nausea
- Dizziness
- Feeling intoxicated
- Sedation/nodding off
- Unsteady gait, slurred speech
- Snoring
- Hypotension
- Slow pulse (bradycardia)
- Shallow breathing (hypoventilation)
- Coma
- Frothing at the mouth (pulmonary oedema)

**Note:** Symptoms may last for 24 hours or more. Death generally occurs from respiratory depression.
• The dispenser must advise the prescriber of the dosing error and record the event.

**Overdose greater than 50% of the normal dose:**

• Advise the patient of the mistake and carefully explain the possible seriousness of the consequences.

• Contact the prescriber immediately. If the prescriber is unable to be contacted, consult a drug and alcohol medical specialist.

• If the prescriber or drug and alcohol specialist decides that the patient requires hospitalisation, the reasons should be explained to the patient and he or she should be accompanied to the hospital to ensure admitting staff receive clear information on the circumstances.

• If the patient has left before the mistake is realised, every attempt must be made to contact him or her.

**Caution:**

• Inducing vomiting may be dangerous and is contraindicated if the patient has any signs of CNS depression.

• Emesis after the first 10 minutes is an unsatisfactory means of dealing with methadone overdose, as it is impossible to determine if the entire dose has been eliminated.

• In circumstances where medical help is not readily available or the patient refuses medical care, induction of vomiting (by mechanical stimulation of the pharynx) within 5–10 minutes of ingesting the dose may be appropriate as a first aid measure only. Ipecac syrup is contraindicated as its action may be delayed.

**Observation:**

Patients in the first two weeks of treatment who receive an overdose of any size require observation for four hours. Observation must continue if there are ongoing signs of intoxication.

Patients who have been on a dose > 40 mg/day consistently for two months will generally tolerate a single double dose without significant symptoms. For a dose greater than double the usual daily dose, the patient will require observation for at least four hours. Observation must continue if there are ongoing signs of intoxication.

If patients are receiving regular takeaway doses, or if they do not attend daily, it cannot safely be assumed that they have been taking their daily dose and have a known level of tolerance. Therefore, such patients require observation in the event of receiving a dose 50% higher than their usual dose.

Patients in whom the level of tolerance is uncertain (dose less than 40 mg/day, or in treatment for less than two months) require observation for at least four hours if they are given a dose 50% higher than their usual dose. Observation must continue if there are ongoing signs of intoxication.

7.5.2.2 Buprenorphine

A patient who receives a buprenorphine dose in excess of that prescribed is not at the same risk of overdose as with methadone and other opioids. If an excess dose has been dispensed:

• Notify the patient and prescriber.

• Warn the patient of the possible effects (drowsiness, nausea, headache).

• Warn the patient of the risks associated with extra drug use, and warn against driving or operating machinery.

• Monitor the patient for at least six hours if:
  — the patient is showing signs of toxicity, such as sedation
  — has commenced treatment in the last two weeks
  — the dose administered is 16 mg or more, given to a patient whose normal dose is 4 mg or less.
  — a dose of 64 mg or more was administered.

• The prescriber should review the patient before the next dose.

7.6 Use of high-dose methadone

There are anecdotal reports that some patients require very high doses of methadone for successful maintenance. However, there is no systematic evidence to support the greater efficacy of doses above 150 mg. The prescribing of very high doses raises several concerns:

• The prescriber may have unrealistic expectations that very high doses may suppress use of non-opioid drugs (such as benzodiazepines).

• There may be an increased risk of diversion with high doses.

• High doses have been associated with potentially fatal arrhythmias, probably in association with prolongation of the QT interval.

It has been demonstrated that in patients who rapidly metabolise methadone, split dosing is more effective in stabilising withdrawal symptoms than the use of higher doses. These concerns make it good practice to obtain a second opinion if considering prescription of high doses.

The referral for a supporting opinion should include the following information:

• current dose
dose proposed
current medications
current drug use
reasons for believing dose increase is appropriate
trough methadone blood concentration (date of test, dose at time)
• number of takeaway doses
• observations 2–3 hours post dose
• results of recent urine toxicology
• recent electrocardiogram with corrected QT interval (QTc)

Prolongation of the QTc is an indication for reducing methadone dose.

The assessment of the patient should include assessment of drug use (including examination for injecting sites), mental state examination, review of side effects, history suggestive of sleep apnoea, and general health issues.

To prescribe a methadone dose above 200 mg/day, approval must be sought through the Pharmacotherapy Credentialling Subcommittee, NSW Health. (Use form given in Appendix M on page 160).

7.7 High-dose buprenorphine

Most patients will be stabilised on buprenorphine doses of 10–16 mg per day. Prescribers should maintain an index of suspicion that requests for higher doses may reflect poor absorption of the drug or the possibility of diversion. If patients complain that doses of 16 mg per day are inadequate, it is judicious to administer a test dose under supervision (checking for technique), then review the patient after 24 hours.

The administration of buprenorphine in doses greater than 32 mg has not been systematically studied. There is no evidence for the greater efficacy of doses above 16 mg at present, and high dose buprenorphine also brings potential problems of diversion. High doses of buprenorphine are expensive. There is no evidence of cardiotoxicity, and there is currently no value in measurement of blood levels of buprenorphine. Clinical assessment, supported by urine toxicology, is required in considering whether to use doses over 32 mg.

To prescribe a buprenorphine dose above 32 mg/day, approval must be sought through the Pharmacotherapy Credentialling Subcommittee, NSW Health. (Use form given in Appendix M on page 161).

7.8 Managing difficult behaviour

At the beginning of treatment, patients sign a Treatment Agreement (Appendix M, page 163) that specifies the conditions under which they will be treated. It may be necessary to remind patients of their obligations under this agreement from time to time. Patients attending the Opioid Treatment Program often exhibit difficult behaviour and staff need to be skilled in handling this. Staff training in aggression management is recommended.

The Treatment Agreement states:

Clients who do not comply with the conditions of methadone/buprenorphine programs in NSW will have their place on the methadone/buprenorphine program reviewed.

The following actions will be taken sequentially when clients do not comply with conditions of the program:

1 A formal warning will be given.
2 A change in conditions of program will occur, including removal of takeaway doses and the requirement to attend more frequent appointments.
3 Transfer to a more supervised treatment setting or to another treatment program.
4 Withdrawal from the program.

Certain actions, namely violence or threat of violence against staff or other patients, property damage or theft from the methadone/buprenorphine program, drug dealing on or near treatment premises, and repeated diversion of methadone/buprenorphine may warrant immediate discharge from treatment.

Sometimes miscommunication or inarticulateness can be interpreted as an act of aggression. Staff must be skilled at dealing with individuals who have limited capacity to express frustration in more usual ways.

When confronted with challenging behaviour, de-escalation may be sufficient to manage the situation. Staff should remain calm, listen to the individual’s concerns in an empathic, non-confronting manner, emphasising their desire to help and try to make the individual more comfortable. Staff should feel able to call for backup or leave the scene at any time they think necessary.

All staff should carry personal duress alarms so that help can be summoned immediately should situations escalate out of control.

NSW Health has a “zero tolerance policy” in relation to violence. Health workers are not required to tolerate violence or the threat of violence from patients or others. Equally, patients should not be expected to tolerate verbal or other violent behaviour from staff. The NSW policy details methods for reducing the risk of violence in the workplace and explains how to manage violent incidents.

7.9 Managing attempts to divert doses

Patients may be tempted to divert doses for use at another time, for use by another person, or for sale. Attempts to divert doses are a breach of the treatment agreement.

Appendix P (page 166) shows an example of a standardised approach to managing attempted diversion of doses of buprenorphine.
7.10 Managing inpatients

If an opioid dependent person is admitted to hospital, the prescribing of methadone, buprenorphine or other opioid drugs may need to be considered, either as continuation of an opioid treatment program, as treatment of opioid withdrawal, or for relief of pain.

7.10.1 Legal restrictions on prescribing drugs of addiction

Under the provisions of Section 28 of the Poisons and Therapeutic Goods Act 1966 (NSW), a medical practitioner may not prescribe any drug included in Schedule 8 of the Poisons List for a person who in his/her opinion is a drug-dependent person without the approval of the Pharmaceutical Services Branch of NSW Health. This legislation is intended to prevent people with drug dependence “shopping around” for drugs and receiving treatment for opioid addiction from more than one prescriber concurrently.

Drugs of addiction included in Schedule 8 of the Poisons List are listed in Appendix Q (page 169). The most recent information can be found at: <www.health.nsw.gov.au/public-health/psb/publications/pdf/drugsofaddiction_schedule8.pdf>.

An exemption from this requirement is provided for inpatients of public hospitals, who may be prescribed a drug of dependence for up to 14 days even when the patient is known or suspected to be drug-dependent.

7.10.2 Treatment of an inpatient currently on methadone or buprenorphine treatment

In general, methadone or buprenorphine treatment should continue in hospital. It is not appropriate for a hospital to withhold methadone or buprenorphine treatment or attempt detoxification of a patient without the specific consent of the patient. The hospital medical officer managing the patient should consult with the prescriber regarding the patient’s opioid treatment.

When patients on methadone or buprenorphine treatment are admitted to hospital, the hospital medical officer can take over prescribing the patient’s opioid treatment for up to 14 days. On admitting the patient, the hospital medical officer should:

• Verify the patient’s identity.

• Identify the authorised prescriber and the patient’s dosing location (either through the patient or by contacting the PSB of NSW Health on (02) 9879 5246 during business hours).

• Contact both the prescriber and the patient’s dosing location to confirm the current prescribed dose, the date and time of the last dose, and whether the patient has been given any takeaway doses. The dosing information must be established to avoid administering an overdose.

If the patient is unable to provide the name of the prescriber and/or dosing location and contact cannot be made with the PSB, a drug and alcohol medical specialist should be consulted for an expert opinion on the advisability of methadone or buprenorphine treatment.

Patients taking methadone are unlikely to exhibit withdrawal symptoms until more than 24 hours after their last dose. If the patient shows withdrawal symptoms and neither the authorised prescriber nor the administration point can be contacted, the patient should be administered 30 mg of methadone orally and further doses up to a maximum of 40 mg daily, titrated against observable withdrawal symptoms, until such time as contact can be made with the prescriber or dosing location.

Patients taking buprenorphine are unlikely to exhibit withdrawal symptoms for two or more days after their last dose. If the patient shows withdrawal symptoms and neither the authorised prescriber nor the administration point can be contacted, the patient should be administered 4 mg of buprenorphine sublingually and further doses, titrated against observable withdrawal symptoms, until such time as contact can be made with the prescriber or dosing location. However, buprenorphine should not be given until the impact on analgesia has been considered. Buprenorphine’s partial agonist properties and strong binding to the μ receptors complicate analgesic use if patients have a condition requiring potent analgesia or pending surgery. Alternatives for these patients include methadone or medications to treat

Further information

withdrawal symptoms such as clonidine, antiemetics and antidiarrhoeal agents.

In the event of emergency department or non-inpatient attendance, it must be understood that a missed dose is not a medical emergency. It is generally not appropriate to prescribe methadone or buprenorphine in the emergency department.

7.10.3 Patients with takeover doses who are admitted to hospital

Patients who have takeover doses for the days they are in hospital should be requested to hand the takeover doses to the ward staff and have their methadone or buprenorphine dispensed through the hospital pharmacy. This allows closer monitoring of their clinical condition and certainty about the dose an inpatient is receiving.

If methadone or buprenorphine is not available from the hospital pharmacy, the prescribed takeover dose may be administered to the patient, provided that the takeover dose is verified and there is no evidence of tampering with the container. Takeover doses must be stored and dispensed by the hospital or removed from the hospital. Takeaway doses should not be given back to the patient on discharge unless by arrangement with the patient’s authorised prescriber.

Patients who refuse to hand over takeover doses should not be given methadone or buprenorphine from hospital supplies. Patients must not leave takeover doses in an unsafe or insecure place (eg, their locker), as methadone and buprenorphine are Schedule 8 drugs and must be stored accordingly. They should be asked to leave the doses at home and have them brought in daily by their relative or friend who should hand it to hospital staff for supervised dispensing.

Patients taking takeover doses in hospital should be monitored for evidence of intoxication or withdrawal, and these should be treated appropriately.

A drug and alcohol medical specialist should be consulted if there are concerns about the patient’s clinical condition. If a drug and alcohol medical specialist is unavailable contact the NSW Drug and Alcohol Specialist Advisory Service (24 hour clinical phone service for health professionals) on (Country) 1800 023 687 or (Sydney) (02) 9361 8006.

7.10.4 Acute pain management in hospital for patients on methadone or buprenorphine treatment

Patients on methadone or buprenorphine treatment who are experiencing acute pain in hospital often have their pain undertreated. Analgesia (including injectable analgesia) should be provided for these patients as for other patients. Opioid analgesics should not be withheld for fear of creating problems of addiction when patients have acute severe pain in the hospital setting. In this situation, opioids in addition to the patient’s usual methadone or buprenorphine dose may be prescribed to relieve pain.

Because of their tolerance of opioids, patients taking methadone or buprenorphine may require larger doses of analgesia for adequate pain relief, but the initial dose and route of administration should be that normally prescribed in the circumstances. Buprenorphine may limit the usefulness of further opioids due to its high affinity for the μ receptor. If analgesia is not achieved, consult practitioners with appropriate expertise in pain management. Consulting a drug and alcohol medical specialist or nurse practitioner may also be helpful.

It may be possible and convenient to provide pain relief for some patients by temporarily increasing their dose of methadone or buprenorphine. With buprenorphine, there is little additional analgesic effect at doses beyond 24 mg in most users. There is some suggestion that providing buprenorphine in divided doses may enhance its analgesic effectiveness.

Severe pain and buprenorphine: Because buprenorphine is a partial agonist, there is a plateau in effect above which dose increases will not increase pain relief. Therefore in cases where the patient has severe pain, it is preferable to stop buprenorphine and induct the patient onto a full agonist opioid drug. If possible, an oral preparation should be used, with dosages titrated to pain symptoms. Clinicians should be mindful to observe for signs of toxicity when transferring the patient onto a short acting full agonist opioid: use 4–6-hourly dosing and review until baseline 24-hour requirements are determined. This dose can then be given as regular divided doses and tapered to permit transfer back to buprenorphine when the pain dissipates. If pain is localised, local/regional blockade should be considered. If the patient may be in pain for several months or more but remains at risk of illicit opioid drug use, a transfer to high dose methadone may be appropriate.

Concerns about creating problems related to opioid dependence arise when patients take opioid analgesics for a protracted period (longer than normally expected for the condition being treated). The management plan for patients requiring ongoing analgesia should be documented in the patient’s medical records, and should include plans for reducing the frequency and/or amount of the analgesic dose. This documentation should be included in the discharge summary provided to the methadone or buprenorphine treatment prescriber.

7.10.5 Responsibilities of the dosing location or prescriber

When a prescriber or a staff member at a dosing location is contacted regarding inpatient treatment of a person in an opioid treatment program, they should recognise that the hospital medical officer may be inexperienced in the treatment of opioid dependent people. They should take all possible steps to ensure that he/she is assisted. This includes, but is not limited to, providing the following information:

- The necessary steps to be taken to comply with legal requirements regarding methadone or buprenorphine treatment, including steps to be taken on discharge.
• The history and progress of the patient — in particular, information regarding his/her reliability and stability, maintenance dose and likely pain relief needs.

• Advice about dosage regimens and the significance of dose changes (Is it high or low? What is the range?), which should, if possible, be documented in the patient’s hospital notes.

The senior registered nurse or pharmacist at the dosing location should document that the patient has become an inpatient and is being dosed elsewhere. To avoid double dosing, he/she should confirm that the patient has been discharged and confirm the date on which the patient last received a dose before recommencing dosing. When a prescribing doctor is contacted regarding treatment, he/she must ensure that the dosing location has been notified.

7.10.6 Treating opioid dependent inpatients not currently in an opioid treatment program

Opioid dependent people who are not in an opioid treatment program may experience withdrawal if admitted to hospital. As a result, some leave hospital against advice, or become agitated and aggressive with staff, or self-medicate with unsanctioned drugs that can confuse assessment and treatment. Adequate treatment of opioid withdrawal in hospital minimises patient discomfort and simplifies management of the patient.

Methadone or buprenorphine may be used to treat withdrawal symptoms if:
• withdrawal symptoms could reasonably be expected to interfere with the optimum medical management of the patient, or
• if the patient is suffering from a serious or life-threatening illness and the patient’s premature self-discharge before completion of therapy would prejudice optimum management.

If methadone or buprenorphine is used to control withdrawal symptoms, the patient must be advised that this does not constitute entry to an opioid treatment program. Entry to a program must be through an approved prescriber.

The aim is to treat withdrawal symptoms and then withdraw methadone or buprenorphine completely before the patient is discharged from hospital. If this is not possible, or if it is considered appropriate to extend the use of methadone after discharge, arrange for continuation by consulting with an approved methadone prescriber. This should be done well in advance of the patient’s discharge.

7.10.6.1 Methadone

If methadone is prescribed for the treatment of opioid withdrawal symptoms in an inpatient not on a methadone program, 10–20 mg in oral liquid form should be administered twice daily initially and gradually increased if necessary until the patient’s condition is stabilised.

Once stabilised, methadone is withdrawn by a regular reduction of the daily dose. A usual reduction regimen is to commence at 30 mg per day of methadone and reduce the dose by 2.5 mg per day. The aim is to withdraw methadone completely before the patient is discharged from hospital. If this is not possible, or if it is considered appropriate to extend the use of methadone after discharge, arrange for continuation by consulting with an approved methadone prescriber. This should be done well in advance of the patient’s discharge.

7.10.6.2 Buprenorphine

Buprenorphine is a relatively safe choice for treating patients with an unknown level of opioid tolerance. It may not be suitable for patients with a high level of opioid dependence who require significant analgesia or are awaiting surgery, who may be better treated with methadone. (Methadone is also preferable in patients who may be pregnant — see section 7.12.1 on page 74.)

This table is given as a guide only, and considerable individual variation in withdrawal severity and medication requirements should be expected. See section 7.10.2 (page 70) regarding hospital prescribing.

<table>
<thead>
<tr>
<th>Proposed inpatient withdrawal regimen</th>
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<tr>
<td>Day 1</td>
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<td>Day 3</td>
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<td>Day 4</td>
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<td>Day 5</td>
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<td>Day 6</td>
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</tbody>
</table>

Do not increase methadone doses above 40 mg daily unless a drug and alcohol medical specialist, drug and alcohol nurse practitioner or other medical practitioner experienced in the management of drug dependence has been consulted.

Proposed inpatient withdrawal regimen
7.11 Patients requiring pain relief

7.11.1 The opioid dependent person presenting with acute pain

Examples include the opioid dependent person (heroin user, not on methadone) with acute pain, who might be hospitalised as a result of trauma, undergoing surgery, or presenting to a primary care setting with an acute painful condition such as a sprain.

Their management in hospital is described in section 7.10.6 (page 72).

In primary care settings, for patients not being referred to hospital, there is seldom occasion to prescribe or administer opioids (and the doctor can explain, correctly, that opioids cannot be prescribed to drug dependent people without the prior authority of the NSW Department of Health). It may be an opportunity to refer the patient to an opioid treatment program, while managing pain with non-opioids. In the rare situations in primary care where people have severe acute pain, humane considerations dictate that opioids may be administered.

7.11.2 Patients on methadone or buprenorphine treatment with acute pain

In primary care settings, acute pain relief is initially managed as it would be for patients who are not opioid dependent. Review and titration of analgesia is determined by the response. See section 7.10.4 (page 71) for the management of such patients in hospital.

Management of such patients is complex and should not be entered into lightly. Most patients prescribed opioids for pain management do not become dependent and those who do may well be reflecting other factors that need to be attended to rather than simply seeing them as individuals who need more or less of a particular medication. In seeking to optimise the approach to the management of chronic pain, the following 10-step protocol is suggested.

<table>
<thead>
<tr>
<th>Ten step chronic pain management protocol</th>
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<tbody>
<tr>
<td>1 Make a diagnosis with an appropriate differential.</td>
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<tr>
<td>2 Undertake psychological assessment, including risk for addictive disorders.</td>
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<tr>
<td>3 Obtain informed consent.</td>
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<tr>
<td>4 Establish a treatment agreement, as these can help clarify appropriately set boundary limits.</td>
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<tr>
<td>5 Do a pre- and post-intervention assessment of pain level and function.</td>
</tr>
<tr>
<td>6 Undertake an appropriate trial of opioid therapy plus or minus adjunctive therapy when other therapies on their own have failed to control pain.</td>
</tr>
<tr>
<td>7 Re-assess pain score and level of function.</td>
</tr>
<tr>
<td>8 Regularly assess the four “A”s of pain medicine: Analgesia, Activity, Adverse effects and Aberrant behaviour.</td>
</tr>
<tr>
<td>9 Periodically review pain diagnosis and comorbid conditions including addictive disorders.</td>
</tr>
<tr>
<td>10 Be meticulous in documenting your management of the patient.</td>
</tr>
</tbody>
</table>

7.11.3 The opioid dependent person with chronic pain

Opioid dependent people with chronic pain are often taking prescribed opioids such as Panadeine Forte, Kapanol, Oxycontin or injectable pethidine or morphine and manifesting clear signs of dependence. It is reasonable to suspect that many people taking opioids for chronic pain have become dependent on opioids, and dependency is playing a part in maintaining the degree of pain and dysfunction which the patient is experiencing. However, there are some circumstances in which the suspicion of dependence becomes more certain — such as people taking escalating doses with diminishing relief of distress, claiming to have lost prescriptions, obtaining prescriptions from multiple prescribers, or injecting tablets designed for oral administration. Such people are demonstrably not in control of their drug use. Enrolling such patients in an opioid treatment program is an appropriate way to supervise and stabilise their drug use.

7.11.4 The patient on methadone or buprenorphine treatment with chronic pain

There is some evidence that chronic opioid administration reduces people’s threshold for experiencing pain, and increases somatic focusing; therefore, one might anticipate that people in an opioid treatment program could be at higher risk of chronic pain states. The treatment of chronic pain is primarily behavioural and psychological, aimed at increasing activity and minimising disability. This should be the focus of management. Since one objective of methadone or buprenorphine treatment is to increase opioid tolerance and blunt the response to additional opioids, it is not appropriate to prescribe additional opioids for chronic pain.

Optimal management is complex, and such patients may require specialist referral.
7.12 Pregnancy and breastfeeding

Pregnant women who use opioid drugs such as heroin are at an increased risk of developing complications in pregnancy, including:

- premature labour and birth
- intrauterine growth retardation
- miscarriage
- intrauterine infection
- antepartum and postpartum haemorrhage
- intrauterine hypoxia or anoxia.

These complications are generally a result of:

- inadequate antenatal care
- lifestyle factors, including smoking, poor nutrition, poor dentition, high levels of stress and deprivation
- repeated cycles of intoxication and withdrawal, which can harm the fetus or precipitate premature labour or miscarriage.

The newborn from these pregnancies are at higher risk of experiencing:

- neonatal abstinence syndrome (NAS)
- sudden unexpected death.

Parents in the Opioid Treatment Program should be advised not to co-sleep with infants, particularly if taking additional sedating substances. Evidence suggests that many unexpected deaths of infants are the result of suffocation while the infant is co-sleeping with another family member. It is recommend that written information is given to the parents on safe sleeping practices.

Acute opioid withdrawal during pregnancy carries particular risks, including miscarriage, premature labour and fetal hypoxia and distress. Specialist care by an obstetrics team in combination with drug and alcohol specialists is required to manage opioid withdrawal in pregnancy.

Methadone or buprenorphine maintenance treatment:

- helps stabilise drug use and lifestyle
- reduces or eliminates illicit opioid drug use and can help stabilise the in utero environment
- facilitates access to comprehensive antenatal and postnatal care
- does not increase the risk of congenital abnormalities in the fetus.

7.12.1 Contraindication to buprenorphine in pregnancy

Approximately 365 cases of babies born to pregnant women maintained on buprenorphine have been reported in the literature, with NAS being the most significant adverse event related to buprenorphine. A number of other adverse events have been reported, including fetal deaths, minor malformations, convulsions followed by cerebral palsy, intrauterine growth restriction and delayed muscular development. However, in all reports buprenorphine has not been implicated as a major aetiological factor; other significant exposures or risks (eg, other substance use, use of other medications) are more likely causes of these adverse events.

Buprenorphine is not recommended for pregnant women and breastfeeding women at present because evidence for its safety is limited. As most women who are candidates for buprenorphine maintenance treatment are in the child bearing years, the initial assessment must consider:

- Are they breastfeeding?
- Might they be pregnant?
- If pregnant, what are their plans for the pregnancy?
- If not pregnant, do they intend to become pregnant?
- If not wishing to become pregnant, what contraception are they using?

Women undergoing assessment for buprenorphine treatment should be provided with information about buprenorphine in pregnancy and breastfeeding. Written informed consent for buprenorphine treatment should include acknowledgement by the patient that buprenorphine is not recommended for maintenance treatment during pregnancy or breastfeeding. Patients should be advised to take contraceptive precautions and be requested to inform staff as soon as possible if they become pregnant.

Women who are on buprenorphine and become pregnant should be advised to consider a transfer to methadone if continuing maintenance treatment, but they should not be compelled to make this change. The transfer should be undertaken carefully to ensure opioid withdrawal is not precipitated. The transfer to methadone from buprenorphine in pregnant women should be undertaken under the supervision and monitoring of a specialist high-risk antenatal service with drug and alcohol support. If a woman declines to transfer to methadone, the insufficient evidence of safety of buprenorphine in pregnancy should be explained in detail, and she should be asked to sign an informed consent form (see Appendix R on page 170).

7.12.2 Contraindications to buprenorphine–naloxone in pregnancy and lactation

Pregnant women who choose to continue buprenorphine treatment should not take the buprenorphine–naloxone combination, as naloxone may have potential adverse affects on the fetus) and the safety of the combined product in breastfeeding has not been established.

As set out in national guidelines, women who become pregnant while on buprenorphine–naloxone maintenance should be switched to either methadone or to buprenorphine. If a
stable patient receiving unsupervised buprenorphine–naloxone dosing becomes pregnant, it may be appropriate to continue unsupervised dosing using buprenorphine, but increasing the frequency of clinical reviews in view of the change in her health status.

7.12.3 Methadone maintenance in pregnancy and breastfeeding

Opioid dependent pregnant women who wish to be treated with methadone should have priority access to a methadone treatment program.

While a methadone program is not the only treatment option available for these women, it is often the most acceptable treatment to the patient and, in most cases, does provide safer and more stable conditions for the pregnancy. If a pregnant woman uses opioids less than three times per week, has been using opioids for less than three months or has been using very small quantities of opioids, then other treatment options could be considered in consultation with her.

7.12.3.1 Starting methadone maintenance

The decision to start methadone treatment of a pregnant woman involves careful assessment of the risks associated with continuing drug use and, when there is some uncertainty about the level of opioid dependence, the risks associated with treating her with a dependence-forming opioid drug.

Methadone is classed as a Pregnancy Category C drug because of the potential risk of respiratory depression in the neonate and the likelihood of neonatal withdrawal syndrome. However, experience has shown that respiratory depression is not a significant problem in babies born to opioid dependent mothers receiving methadone maintenance treatment.

7.12.3.2 Management in pregnancy

Pregnant women should be maintained on an adequate dose of methadone to achieve stability and prevent relapse or continued illicit opioid drug use.

Women already in methadone treatment who become pregnant can continue in treatment. The bioavailability of methadone is decreased in the later stages of pregnancy due to increased plasma volume, an increase in plasma proteins that bind methadone, and placental metabolism of methadone. It may be necessary to divide the daily dose and possibly to increase the dose in the late second or third trimester of pregnancy to avoid withdrawal symptoms and minimise additional drug use.

Antenatal and postnatal care should be managed in collaboration with a specialist obstetric service experienced in the management of drug use and/or dependency during pregnancy.

7.12.3.3 Dose reductions or detoxification during pregnancy

Patients may wish to reduce their methadone dose or withdraw from treatment before giving birth. Opioid withdrawal in the first trimester of pregnancy is thought to be associated with an increased risk of premature labour. In the third trimester it may be associated with fetal distress and death. Therefore, it is important that pregnant women are not exposed to withdrawal during the first and third trimesters.

If dose reductions or detoxification are to be undertaken during pregnancy, they should be implemented in the second trimester. A cautious approach is essential:

- Dose reductions should only occur if the pregnancy is stable.
- Hospitalisation could be considered for a period of time.
- The magnitude and rate of reduction needs to be flexible and responsive to the symptoms experienced by the woman concerned.
- Withdrawal symptoms should be avoided as much as possible as they cause considerable distress to the fetus.
- Careful monitoring of the pregnancy and fetus should be undertaken during dose reduction.
- In most instances, dose reductions of 2.5–5 mg per week are considered safe.

Some women insist on reducing their methadone dose during the first or third trimester even against medical advice. In such cases, a slow reduction (2.5 mg per week) is recommended, with careful monitoring for any signs or symptoms of withdrawal, especially in the first three months of the infant’s life.

The prescriber should advise the patient against withdrawing in the third trimester. If the patient insists, she should be given detailed advice about the risks of withdrawal, and asked to sign a form indicating that she is undertaking a withdrawal regimen against medical advice.

7.12.3.4 Breastfeeding

Breast milk contains only small amounts of methadone or buprenorphine and mothers can be encouraged to breastfeed regardless of their methadone/buprenorphine dose provided that they are not using other drugs.

Breastfeeding may reduce the severity of the neonatal withdrawal syndrome. If the mother is on a high dose of methadone/buprenorphine and the baby is weaned suddenly, the baby may show signs of NAS. This is not often seen, but is more likely if the baby is less than three months of age.
7.13 Neonatal withdrawal

Babies born to mothers on methadone maintenance treatment may experience a withdrawal syndrome. Available evidence gives little support to the existence of a simple relationship between the severity of the neonatal withdrawal syndrome and maternal methadone dose at delivery, and its occurrence is unpredictable. The benefits of methadone maintenance treatment for both the mother and the baby outweigh any risks from the neonatal withdrawal syndrome.

Severities of withdrawal is probably ameliorated if neonates can be kept with their mothers rather than in the neonatal intensive care nursery, which may be stressful and overstimulating. However, this is not always possible.

All babies born to opioid dependent mothers should be observed by experienced staff for the development of withdrawal signs. A validated scale should be used to assess the presence and severity of neonatal withdrawal (see Appendix S on page 171).

Common signs include:
- irritability and sleep disturbances
- sneezing
- fist sucking
- a shrill cry
- watery stools
- general hyperactivity
- ineffectual sucking
- poor weight gain
- dislike of bright lights
- tremors
- increased respiration rate

Less common signs include
- yawning
- vomiting
- increased mucus production
- increased response to sound
- convulsions (rare).

Monitoring should be repeated every four hours and conducted after feeding if possible, when objective signs of withdrawal will be clearest. Withdrawal symptoms usually start within 48 hours of delivery but may be delayed for up to 14 days in a small number of cases. Experience in the United States suggests that in cases where withdrawal is delayed it may be because methadone was being used in conjunction with illicit benzodiazepines and the infant is withdrawing from the benzodiazepines.

Treatment of neonatal withdrawal is being considered by an expert group of Australian neonatologists and guidelines on management are being developed.

Supportive treatment involves minimizing environmental stimuli and enhancing the baby’s comfort and may include:
- soothing by holding close to the body or swaddling
- keeping nostrils and mouth clear of secretions
- use of a dummy to relieve increased sucking urge
- frequent small feeds
- skin to skin contact when feeding.

Treatment with morphine should be considered for infants who exhibit severe signs of withdrawal:
- seizure
- weight loss (poor feeding, diarrhoea and vomiting, dehydration)
- poor sleep
- fever.

Treatment with morphine may depress respiration and should be used with extreme caution. Neonatal care should be managed in collaboration with a specialist obstetric or paediatric service experienced in the management of babies born to drug dependent mothers.

Naloxone should not be used in infants born to opioid dependent women as it may precipitate withdrawal. Mechanical ventilation may be used as an alternative.

Further information


7.14 Child protection

On initial assessment, at treatment review and when assessing eligibility for takeaway doses, it is important to consider the safety and welfare and wellbeing of any children within the patient’s care. This may include a patient’s own children, children living at the same residence, or children to whom the patient has access.

Health care workers have a duty under the Children and Young Persons (Care and Protection) Act 1998 (NSW) to
notify DOCS whenever they suspect that a child or young person may be at risk of harm through abuse or neglect. This duty may be invoked when considering the potential risk of harm of a child yet to be born.

When necessary, the duty to report possible harm through abuse or neglect overrides the duty to maintain patient confidentiality.

Under Section 23 of the Act, a child or young person is at risk of harm if current concerns exist for the safety, welfare and wellbeing of the child or young person because of the presence of one or more of the following circumstances:

- the child or young person’s basic physical or psychological needs are not being met or are at risk of not being met
- the parents or caregivers have not arranged and are unable or unwilling to arrange for the child or young person to receive necessary medical care
- the child or young person has been, or is at risk of being, physically or sexually abused or ill-treated
- the child or young person is living in a household where there have been incidents of domestic violence and, as a consequence, the child or young person is at risk of serious physical or psychological harm
- a parent or caregiver has behaved in such a way towards the child or young person that the child or young person has suffered or is at risk of suffering serious psychological harm.

The name of the child or young person, a description of what has occurred and the grounds for reporting should be provided when making a report.

A parent’s enrolment in an opioid treatment program is not itself a reason to make a report to DOCS.

In relation to newborn infants of mothers on methadone maintenance, NSW Health Policy Directive PD2005_299, Protecting children and young people, recommends that a multidisciplinary case conference should be convened in accordance with the NSW Health neonatal abstinence syndrome guidelines (2005) to formulate a discharge plan for mother and baby with clear, documented responsibilities and timeframes. Representation at this meeting should include the parents, a health worker with expertise in child protection, and any services or supports involved in the family.

7.15 Consumption of methadone or buprenorphine by a child

Methadone and buprenorphine takeaway doses may be inadvertently taken by young children. Methadone may be deliberately administered to them by a patient or other person. Ingestion of methadone can be particularly dangerous for children and is a potentially life-threatening situation. Even the smallest amount can be fatal. Buprenorphine, while safer in adults, can pose a significant risk to children if consumed.

Recommended procedures:

- Assess the level of consciousness and monitor this continuously until the child is in the care of ambulance or other qualified staff.
- Refer the child to a hospital emergency department without delay, providing the information available about the amount taken and the time.
- Administer oxygen if available.
- Consider naloxone administration if the child is showing signs of respiratory depression. Document any treatment given.
- Notify the prescriber and the PSB or the MHDAO of the incident.
- If a child has ingested methadone or buprenorphine by any means, the child has been placed at risk of harm and the authorities should be notified:
  — A report to DOCS should be made (see section 7.14, Child protection, on page 76). Concerns for the child should be discussed with hospital staff.
  — Police may be involved in exceptional circumstances.

7.16 Treatment of adolescents

There is considerable evidence that the age of first drug use is declining. Many adolescents present to treatment services with serious social and psychological problems associated with frequent dangerous drug use. However, most adolescents use multiple drugs, and dependence on heroin alone is extremely uncommon in this age group. Many adolescents use prescription drugs, and may seek opioid maintenance treatment as a potential source of continuing drugs despite having relatively little prior exposure to opioids. When a young person clearly has serious and dangerous

Further information on child protection
7.17 Domestic violence

Prescribers should be alert to the possibility of domestic violence and routinely screen all female patients for risk (see Appendix H on page 128) and make them aware of services to assist.

If a patient reports domestic violence, ongoing assessment of safety and other needs should be made. This assessment should consider both the patient and any children in her care.

In some circumstances it may be appropriate to consider these issues for male patients.

7.18 Patients with coexisting mental health problems

Many opioid users exhibit symptoms of anxiety and depression when they first present for treatment. The prevalence of mental health problems is higher among opioid users than in the general population.

Assessing mental health status should be an integral part of the care of patients in an opioid treatment program. Checking for suicidal thoughts should be a routine part of the risk assessment process because the susceptibility to suicide is higher in the opioid using population than in the population at large.

Most, but not all, studies link psychiatric distress to poorer treatment outcome. Several studies have indicated that methadone or buprenorphine maintenance can reduce levels of psychiatric distress, with improvement apparent within weeks of commencement of treatment.

After stabilisation on methadone or buprenorphine, screen all patients again for psychiatric disorders. A careful and detailed mental state examination will usually suffice.

Psychotherapy as an adjunct to methadone or buprenorphine treatment may benefit patients with medium and high levels of psychiatric problems, but for those with minor psychiatric problems the addition of psychotherapy offers no advantage.

Depression has been found to predict poor psychosocial functioning and to increase the risk of relapse to opioid use in the event of life crises. Evidence of the effectiveness of antidepressants as adjuncts to methadone or buprenorphine treatment is equivocal, with only a few studies demonstrating favourable effects on mood. Consideration could be given to supervised dosing of psychiatric medication if compliance is an issue.

7.19 Patients with HIV

The Opioid Treatment Program should give priority of access to HIV-positive patients and ensure that they have access to specialist HIV medical care so that the patient’s overall health may be monitored and appropriate treatment provided as required. In general, patients who are HIV-positive are able to comply with the conditions of the Opioid Treatment Program, but will require additional services.

Both methadone and buprenorphine have interactions with HIV medications (see Appendix D on page 111 and Appendix G on page 127). Higher doses may be necessary if HIV medications increase methadone/buprenorphine metabolism.

In the terminal stages of AIDS, providers of opioid treatment may need to work with hospice services in managing methadone treatment and AIDS conditions.

7.20 Patients with hepatitis B or C

7.20.1 Hepatitis B

Refer patients who are acutely infected or who are chronic carriers of hepatitis B to a gastroenterologist for specialist assessment and follow-up.

Recommend hepatitis B vaccinations to all patients who are found to have no immunity to the hepatitis B virus.
7.20.2 Hepatitis C

A high percentage of patients entering the Opioid Treatment Program will have been exposed to hepatitis C and will have antibodies to hepatitis C. Most of these will be infectious and will have hepatitis C virus (HCV RNA) circulating.

All drug and alcohol services in NSW should follow appropriate clinical guidelines in relation to hepatitis C, hepatitis B and HIV. It is recommended that all services should:

- Discuss the risk of exposure to all blood borne viruses with their clinic attendees at some point early in their contact with the service.
- Offer the possibility of testing for hepatitis C, hepatitis B and HIV. This testing may need to be done in the local pathology service but arrangements should be made to facilitate accessing the testing mechanism.
- Offer testing for liver function for those with evidence of exposure to hepatitis C or hepatitis B.
- Have staff available (at least on a monthly basis) to discuss test results with patients.

Further information


7.20.3 Impaired liver function

Patients with chronic liver disease on long term methadone or buprenorphine treatment generally do not need dose alterations, but abrupt changes in liver function might necessitate substantial dose adjustments.

7.21 Dosing arrangements for severely ill patients

Some patients may become temporarily or permanently unable to attend their usual dosing location. Options include:

- using another dosing location that may be closer to the patient or provide easier access
- takeaway doses
- dosing at home
- collection of doses by a responsible carer.

7.21.1 Dosing at home

The capacity to provide methadone or buprenorphine treatment to patients at home is limited by the resources available to the service provider. If dosing at home is to be offered:

- the nature and severity of the illness should be medically verified
- a registered nurse and one other responsible person should administer the dose in the patient’s home
- before attending the patient’s home, staff should carefully explore the extent to which their safety may be jeopardised during the home visit. If the administering staff are concerned about their personal safety in a particular patient’s home, home dosing should not occur.

Service providers should have their own procedures for these matters.

7.21.2 Collection of doses by a responsible carer

Before allowing collection of doses by a responsible carer:

- the nature and severity of the illness should be medically verified
- the patient, carer, prescriber, dosing point and other treating practitioners should all agree to this approach
- appropriate procedures for identification of the carer should be employed at the dosing point.

The patient and the dose collection process should be reviewed regularly.

7.22 Multiple dosing locations

Patients may receive methadone or buprenorphine from more than one dosing location in some circumstances. This can be useful, for example, in accommodating patients who work at a location remote from home, and for periodic detainees. This arrangement can also be useful when a dosing location is closed on one or more days of the week.

However, administrative measures have to be carefully planned and monitored to prevent mistakes being made. If this is not done, patients may not receive doses at either site, or may be dosed at both sites on the same day. These procedures are to be followed:

- One site is nominated as the primary dosing site. This will usually, but not always, be the site attended by the patient more frequently, and preferably a private or public clinic
rather than a community pharmacy. The agreement as to who will be the primary dosing site should be documented and available in the case notes at both sites.

- The primary dosing site is responsible for ensuring that the patient is dosed appropriately. This is the responsibility of the senior registered nurse, the prescriber, or the senior pharmacist.

- The days that the patient will be dosed at each site are nominated and generally will be fixed.

- The senior registered nurse of the primary clinic, the prescriber, or the senior pharmacist contacts the secondary dosing site at the beginning and end of each period for which the patient will be presenting at the secondary site.

- When patients are attending dual dosing locations on a permanent basis, each site must have full documentation, including a recent photograph. The days on which the patient is to be dosed at each site are to be clearly marked on the patient’s card.

- The PSB should be advised of the arrangements for dual dosing locations.

Generally patients are not to be dosed at a dosing location other than on the designated day(s). The only exception to this is if the patient is unable to present to the usual dosing location. This may occur, for example, when a patient is not at work on his/her regular days due to illness or holidays. In the case of holidays this is to be arranged in advance.

In other cases, the patient is to contact the dosing location designated for the day and explain the circumstances. The pharmacist or senior registered nurse will then contact the other dosing location and enquire whether the patient could be dosed at that point for that day(s). A note is to be made on the patient’s card that he/she is not to be dosed at the designated site that day.

The pharmacist or senior registered nurse at the dosing location at which the patient is to be dosed must verify the identity of the caller. This will usually be done by calling back.

If any doubt exists as to whether the change of arrangement may result in double dosing, the dose is to be withheld. Regular communication should occur between both dosing locations to ensure safety and monitor the patient’s progress.

### 7.23 Gambling

Studies have found that rates of problem or pathological gambling are higher among individuals seeking treatment for drug and alcohol problems than in the general population. Toneatto and Brennan (2002) reported a rate of 10.5% in their sample of treatment seeking substance users. This compares with rates of between 1.5% and 3% reported in the general population. Some argue that high rates of comorbidity support an addiction model of pathological gambling. However high rates may also be explained by the co-location of alcohol and gambling opportunities.

#### Further information

- G-Line on 1800 633 635 is available to professionals and patients for information about gambling problems.
- Blaszczynski A. To formulate gambling policies on the premise that problem gambling is an addiction may be premature. *Addiction* 2005: 100: 1230-1232.

### 7.24 Justice Health settings

Patients who are in an opioid treatment program when they enter prison or a juvenile detention centre will have their treatment continued unless clinically contraindicated.

Other people may begin methadone or buprenorphine treatment while in a correctional setting. The indications for treatment are the same as in the community setting.

The transition from detention to the community involves a risk that the patient will return to illicit opioid use. After release from the correctional setting, patients should have priority access to public dosing and case management in the Area Health Service to which they are released regardless of:

- where they started on an opioid treatment program (in a correctional centre or in the wider community)
- whether they had a public or private point of entry to methadone or buprenorphine treatment.

The Justice Health Statewide Drug and Alcohol Discharge Planning Service will, where possible, negotiate with the relevant community-based treatment program before releasing a patient on methadone or buprenorphine maintenance. Because of the way that the court system operates, in some instances a patient may be released directly from court without Justice Health staff being informed. This will result in an “unexpected release” which will mean that no transfer of care has been prearranged. In these instances the community based service provider should contact Justice Health Statewide Drug and Alcohol Discharge Planning Service on (02) 9289 5949 or 02 9289 5948 so that appropriate arrangements can be made for these patients.

A comprehensive treatment plan (see section 4.3 on page 30) should be developed collaboratively between the treatment team, the patient and community providers of opioid treatment, preferably before release. In-reach workers can greatly facilitate this process.
Patients newly released from prison or juvenile detention should be maintained in public dosing until clinically stable and assessed as suitable for private sector dosing. Where no convenient public dosing points exist on release from prison, or if it is not in the best interests of the patient to be publicly dosed, the Area Health Service should:

- take responsibility for identifying and arranging alternative treatment
- discuss the patient’s requirements with Justice Health.

If a person was treated in a specific opioid treatment program before incarceration and chooses to return, that program should take the patient back into treatment after release. If this results in the program temporarily exceeding its authorised limit of patients, then it should return to its authorised numbers by attrition from the program over time.

**Justice Health prescriptions**

- A prescription can only be altered by the person who has issued it.

- Patients should have their care transferred to a community-based service provider within four weeks of release from prison. If a patient becomes clinically unstable after release and is still on a Justice Health prescription, then the community-based service provider should arrange transfer of care so that the treatment plan can be altered according to the clinical indications.

**7.24.1 Choice of methadone or buprenorphine in Justice Health settings**

It is NSW Health policy that buprenorphine–naloxone therapy not be initiated for patients in correctional settings. However, patients who are receiving buprenorphine–naloxone on entry into a correctional setting will be maintained on this treatment.

Prisoners who are assessed as being at high risk of relapsing into heroin use upon release from prison will be offered methadone maintenance treatment in the first instance. Methadone is the first line of treatment in the correctional setting.

Because buprenorphine administration is resource intensive, it potentially affects the availability of other health interventions in correctional settings. Therefore, there is a limit on the number of patients who can receive buprenorphine treatment at each correctional setting. Patients requesting buprenorphine treatment or transfer from methadone to buprenorphine can only do so when this limit will not be exceeded.

**7.25 Patients under legal supervision**

Public and private opioid treatment services are responsible for dosing any of their patients who are being held in police custody, except for patients held in cells where Corrections Health nurses are available to do the dosing. The police should inform the relevant service provider as early in the day as possible that a patient will require a dose of methadone that day.

For dosing in cells, the documentation that should be forwarded from the patient’s regular methadone or buprenorphine provider to the service providing the patient’s cell dose must include:

- patient identification, including photograph and/or physical description
- a copy of the prescription/treatment chart for the patient
- verification of the time and date of the administration of the patient’s last dose
- verification of the number of takeaway doses (if any) provided when the patient was last seen for dosing.

The dose should be administered by at least one registered nurse or pharmacist at the cells, who should carefully confirm the identity of the patient before administering the dose and closely observe the patient taking the dose to prevent diversion.

**7.26 Urgent prescriptions due to unforeseen circumstances**

In special circumstances a patient may require a prescription or an authorisation to receive a dose at a location other than their usual dosing site.

If the patient’s regular prescriber cannot be contacted, a locum prescriber can be requested to provide a prescription to cover the special circumstances. If no details can be obtained about an individual claiming to be on methadone or buprenorphine from a prescriber or a dispensing site (public or private) then it is appropriate to refuse to prescribe or provide these drugs.

**7.27 Arrangements for travel**

The transfer of a patient’s methadone or buprenorphine treatment within NSW, between states and overseas should be carried out by the prescriber (or his/her delegate). The necessary documentation for a transfer should be provided by the treating clinician and clinicians from the transfer destination. See section 7.22, Multiple dosing locations (page 79), for procedures to ensure that double dosing does not occur.

The PSB does not require notification of temporary changes in administration point, but should be notified of overseas travel or transfers.

Further information

If overseas travel requires the patient to carry takeaway doses, the prescriber, as well as following the NSW policy regarding takeaway doses, must clarify with the consulates of the intended destinations their position on a foreigner entering in possession of methadone or buprenorphine. Physeptone (methadone) tablets rather than methadone syrup should be considered to avoid breakage or spillage. The prescriber must comply with any special condition on the entry of a person possessing methadone or buprenorphine: providing a letter stating that the person is in possession of the drug to treat a medical condition in accordance with Australian laws is usually adequate. If the destination requires a letter from the Australian Government this must be obtained from the Therapeutic Goods Administration (TGA, phone [02] 6270 4321).

When travelling overseas, takeaway doses should be in their original packaging, with labelling. They should be carried in hand luggage and be declared at customs.

### Further information

Two websites that may assist with overseas travel and dosing are:

- **Maintenance assistance point.**
  <http://www.q4q.nl/methwork/kaart.htm>
  This site is for Europe and has a map.

- **Travel guide index.**
  <http://www.indro-online.de/travel.htm>
  This site is for the whole world and each country is listed alphabetically.
8 Ending methadone or buprenorphine treatment

Chapter summary

- Outcomes of methadone or buprenorphine maintenance improve with increasing time in treatment. It is recommended that patients be encouraged to remain in treatment for at least 12 months to achieve enduring lifestyle changes.

- Patients who leave an opioid treatment program voluntarily after a gradual withdrawal from drug treatment are least likely to relapse into illicit opioid use. Forcing a patient to withdraw from treatment may result in return to opioid use and related problems.

- Elements of successful withdrawal from therapy:
  - Planning and collaboration between patient, prescriber and other staff.
  - Flexible and slow dose reduction. Planned withdrawal can take months.
  - Psychosocial support, such as supportive counselling, information and skills training, close monitoring, residential rehabilitation, family involvement.
  - Aftercare: continuing counselling and involvement of the case manager, careful handover to the patient's general practitioner.

- Sleep disturbance is common among people who withdraw from methadone. Provide information about withdrawal-related symptoms and offer training in non-pharmacological strategies to cope with disturbed sleep.

- Other psychotropic medication (in particular, hypnotics and sedatives) is not recommended, except when indicated for patients with diagnosed psychiatric comorbidity. If sedative/hypnotic medication is prescribed, it should be at a low dose for a specified short duration (3–5 days). Provide supervision in all cases and restrict the quantity of tablets to 1–2 days' requirements for safety.

- The clinician should remain vigilant to the possibility that alcohol consumption or other drug use may increase to hazardous or harmful levels during and after withdrawal from opioids.

- Typical methadone dose reduction regimen:
  - dose above 80 mg/day: reduce by 10 mg per week
  - dose 40–80 mg/day: reduce by 5 mg per week
  - dose below 40 mg/day: reduce by 2.5 mg per week or fortnight

  Typically, patients tolerate dose reduction very well to a certain point, but require slower reductions thereafter.

- Typical buprenorphine dose reduction regimen:
  - dose above 16 mg/day: reduce by 4 mg per week or fortnight
  - dose 8–16 mg/day: reduce by 2–4 mg per week or fortnight
  - dose below 8 mg/day: reduce by 2 mg per week or fortnight.

  Patients on less-than-daily dosing should usually be transferred to daily dosing once their dose has reduced to 8 mg (divide the dose into daily equivalents and continue the reduction regimen with daily review and support).

- Administering naltrexone to a patient who is physically dependent on opioids will precipitate severe withdrawal.

- Patients transferring from methadone maintenance to naltrexone should withdraw completely from methadone and allow a 14-day drug free period before beginning naltrexone treatment.

- Patients transferring from buprenorphine maintenance to naltrexone should withdraw completely from buprenorphine before beginning naltrexone treatment. If the last buprenorphine dose was 2 mg for at least one week, naltrexone can be given 4–5 days later. If the last buprenorphine dose was more than 2 mg, delay starting naltrexone for 7 days.

- Patients who are experiencing difficulty in withdrawing from methadone may find it easier first to transfer to buprenorphine, and then to withdraw from that drug.
- When relapse occurs some time after leaving treatment and the patient seeks readmission to an opioid treatment program, this should be offered expeditiously and without recrimination.  

8.2.7

- Aftercare services might include skills training (eg, relapse prevention, problem solving skills or vocational skills training), social support services (eg, self-help groups such as Narcotics Anonymous), or booster motivational counselling sessions. Supportive care should be offered for at least six months after finishing maintenance treatment.

8.3

- Patients who miss appointments for dosing should be managed according to the procedures in section 7.1 (page 62). Patients who miss dosing appointments for seven or more consecutive days should be considered to have withdrawn from the opioid treatment program.

8.4, 7.1

- Under the treatment agreement signed by all patients, patients may be removed from the Opioid Treatment Program for:
  - violence or threat of violence against staff or other patients
  - property damage or theft from the clinic or dosing location
  - drug dealing on or near the clinic or dosing location
  - diversion of doses
  - unacceptable disruption to the local amenity.

8.5

- Dose reduction should be gradual. Rapid dose reduction or abrupt cessation of treatment is warranted only in cases of violence, assault or threatened assault.

8.5.3

- All patients should have access to procedures for response to conflicts between themselves and their treatment providers.

8.6

- When a patient exits an opioid treatment program, or transfers between prescribers, a Treatment Exit Form (available from the Pharmaceutical Services Branch [PSB]) must be completed and must be immediately forwarded to the PSB. Patients must be exited from treatment with one prescriber to begin treatment with another.

8.6

- If a patient has not changed prescriber but is to transfer between dosing sites, the PSB is to be notified by phone immediately of the change. To avoid the potential for double dosing, the prescriber should notify the previous dosing site and have them cancel all scripts.

8.6

- No prescriber may refuse to complete exit procedures for a patient.
8.1 Time in treatment

Outcomes of methadone or buprenorphine maintenance improve with increasing time in treatment. Studies of methadone maintenance treatment have found that:

• a sustained reduction in heroin use after treatment was only observed for those who spent more than one year in treatment.

• significant reductions in criminality were only observed while patients remained in treatment.

• it is a combination of treatment duration and behaviour change (ceasing heroin use, stable relationship, employment) during treatment, which predicts positive outcomes after treatment.

It is recommended that patients be encouraged to remain in treatment for at least 12 months to achieve enduring lifestyle changes.

8.2 Planned withdrawal

Patients who leave an opioid treatment program voluntarily after a gradual withdrawal from drug treatment are least likely to relapse into illicit opioid use. Successful withdrawal requires planning. The decision to withdraw should be made collaboratively between the patient, the prescriber and the case manager, with information contributed by the pharmacist/dispensing staff. When all agree about the timing and method of withdrawal, patients tend to be more successful in their dose reduction. It remains, however, the patient’s right to withdraw from treatment at any time.

Patients who request to reduce their dose should be supported whenever possible. However, some patients may wish to withdraw from treatment either too quickly or at times of instability (eg, while increasing or regularly using illicit opioids, or while suffering depression). In such cases the clinician’s concerns should be discussed with the patient to develop a mutually agreeable approach to dose reduction if possible.

Relative contraindications to planned withdrawal:

• irregular attendance for dosing

• non-attendance at case review meetings

• current significant psychological or social instability or distress (eg, acute mental health problem, bereavement, homelessness)

• current significant use of illicit opioids or other drugs.

Asking a patient to reduce the dose of methadone or buprenorphine at a time of increasing illicit opioid use is not appropriate. Dose reductions should be planned and achieved during a period of stability and sustained motivation.

Forcing a patient to withdraw from treatment may result in a return to opioid use and related problems. Unless there is a specific reason for involuntary discharge from treatment (see section 8.5 on page 87) this approach is not encouraged.

The elements of treatment that assist patients to complete withdrawal successfully are:

1 Dose

• Take a flexible approach to dose reduction, individualising reduction regimens to best suit each patient.

• Use slow rates of reduction. Planned withdrawal can take months.

• If relapse is likely, or the patient is not coping, suspend dose reductions or even consider an increase in dose.

2 Psychosocial support during withdrawal

• Offer more frequent supportive, skills oriented and relapse prevention counselling.

• Provide accurate information about what the patient is experiencing.

• Provide more frequent monitoring and review.

• Offer access to residential programs if necessary (residential withdrawal or rehabilitation programs, such as WHOS MTAR, the methadone to abstinence residential program provided by We Help Ourselves, www.whos.com.au).

• If possible, involve significant others (including family) in providing support.

3 Aftercare

• Offer continuing services, including counselling, continuing case management and structured group programs after completion of withdrawal.

• Case managers should remain involved in the care of patients who have voluntarily withdrawn for at least three months after completion of withdrawal.

• Encourage/assist the patient to arrange continuing primary care with a general practitioner (and appropriate specialist care for any persisting comorbidity).

8.2.1 The place for adjunctive pharmacotherapy during withdrawal

Sleep disturbance is common among people who withdraw from almost any psychoactive drug, including methadone or buprenorphine. Explain this to patients, provide information about withdrawal-related symptoms and offer training in non-pharmacological strategies to help them cope with disturbed sleep.
Other psychotropic medication (in particular, hypnotics and sedatives) is not recommended, except when indicated for patients with diagnosed psychiatric comorbidity. If it is considered appropriate to prescribe sedative/hypnotic medication, it should be at a low dose for a specified short duration (3–5 days), with prior explanation of the reason for its prescription, the associated risks of taking such medication and the intended short duration of this treatment. Provide ongoing supervision in all cases and restrict the quantity of tablets to 1–2 days’ requirements for reasons of safety.

8.2.2 Avoiding secondary problems with alcohol and sedative/hypnotic drugs

During and after withdrawal from opioids, excessive use of alcohol and the inappropriate use of sedative/hypnotic medication is common. This should not necessarily be construed as indicating a long-term shift to alcohol and other drug dependence, but the clinician should remain vigilant to the possibility that alcohol consumption or other drug use may increase to hazardous or harmful levels and provide appropriate interventions.

8.2.3 Methadone dose reduction

In general, the following rate of methadone dose reduction is well tolerated by patients:

<table>
<thead>
<tr>
<th>Dose reduction regimen for methadone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dose</strong></td>
</tr>
<tr>
<td>Above 80 mg/day</td>
</tr>
<tr>
<td>40–80 mg/day</td>
</tr>
<tr>
<td>Below 40 mg/day</td>
</tr>
</tbody>
</table>

Typically, patients tolerate dose reduction very well to a certain point, but require slower reductions thereafter.

8.2.4 Buprenorphine dose reduction

In general, the following rate of buprenorphine dose reduction is well tolerated by patients who are receiving daily or less-than-daily dosing with buprenorphine:

<table>
<thead>
<tr>
<th>Dose reduction regimen for buprenorphine daily dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dose</strong></td>
</tr>
<tr>
<td>Above 16 mg/day</td>
</tr>
<tr>
<td>8–16 mg/day</td>
</tr>
<tr>
<td>Below 8 mg/day</td>
</tr>
</tbody>
</table>

Studies suggest that gradual reduction is more effective than rapid. More rapid dose reduction may be considered in those who only had a recent brief period of opioid use or when circumstances make rapid dose reduction desirable. More rapid dose reduction on an outpatient basis should only be conducted when there is significant support and opportunity for review.

There is no evidence to support dose reductions in increments below 2 mg using 0.4 mg tablets, since at lower doses buprenorphine’s duration of action increasingly diminishes. However, some patients may benefit psychologically from these lower dosing incremental reductions. Since the withdrawal is likely to be protracted and there is little further reduction in symptom severity, very low dose tapers are not to be routinely used.

All patients should be asked to attend for daily reviews for five days after their last dose of buprenorphine. This allows for monitoring and appropriate treatment of delayed withdrawal, often seen after finishing a course of buprenorphine. If this delayed withdrawal is uncomfortable, the patient should be provided with symptomatic treatment. The option of accessing local home withdrawal support should be discussed with the prescriber, case manager, patient and home detoxification staff.

Most patients will not be comfortable on less-than-daily doses below 8 mg. Once patients on less-than-daily dosing reduce to a dose of 8 mg, it is preferable to transfer them onto a daily dosing equivalent and continue with a daily dosing reduction regimen. This permits closer monitoring during withdrawal, with enhanced support from the case manager. Some patients may wish to remain on alternate day dose reductions, but the offer of a transfer to daily dosing if symptoms of withdrawal become distressing should remain open.
8.2.5 Transferring to naltrexone
Administering naltrexone to a patient who is physically dependent on opioids will precipitate severe withdrawal.

Assess the patient carefully for other opioid use before beginning naltrexone treatment. Administer a naloxone challenge test and confirm by means of appropriate urine screening.

8.2.5.1 Transferring from methadone
Patients transferring from methadone maintenance to naltrexone should withdraw completely from methadone and allow a 14-day drug free period for stored methadone to be eliminated from the body before beginning naltrexone treatment.

Seek specialist advice if it is not possible to follow this regimen.

8.2.5.2 Transferring from buprenorphine
Patients transferring from buprenorphine (or buprenorphine–naloxone) maintenance to naltrexone should withdraw completely from buprenorphine and allow a drug-free period for stored buprenorphine to be eliminated from the body before beginning naltrexone treatment.

• If the last buprenorphine dose was 2 mg for at least one week, naltrexone can be given 4–5 days after the last dose of buprenorphine.

• If the last buprenorphine dose was more than 2 mg, delay starting naltrexone until 7 days after the last dose of buprenorphine.

If the last buprenorphine dose was 2 mg for at least one week, naltrexone can be given 4–5 days after the last dose of buprenorphine.

If the last buprenorphine dose was more than 2 mg, delay starting naltrexone until 7 days after the last dose of buprenorphine.

8.2.6 Transferring between methadone and buprenorphine
Patients who are experiencing difficulty in withdrawing from methadone may find it easier first to transfer to buprenorphine, and then to withdraw from that drug.

For information about transferring from methadone to buprenorphine or from buprenorphine to methadone, see section 4.4.2 (page 31).

8.2.7 Readmission to treatment
When relapse occurs some time after leaving treatment and the patient seeks readmission to an opioid treatment program, this should be offered expeditiously and without recrimination. Provided that the person is clinically suitable for methadone or buprenorphine treatment, there should be no barriers to readmission.

8.3 Aftercare
Clinicians who provide opioid treatment should, whenever acceptable to the patient, offer scheduled aftercare support services themselves or by referral.

Aftercare consists of structured interventions to assist patients who have completed treatment to remain drug-free and improve their psychosocial functioning. Aftercare is aimed at reducing the high rates of relapse after methadone treatment.

There is evidence from randomised controlled trials that structured aftercare is better than assistance on request in reducing the risk of relapse and self-reported crime, and helping unemployed patients find work.

Aftercare services might include skills training (eg, relapse prevention, problem solving skills or vocational skills training), social support services (eg, self-help groups such as Narcotics Anonymous), or booster motivational counselling sessions.

Supportive care should be offered for at least six months after finishing methadone or buprenorphine treatment.

Providing such aftercare to those who are highly motivated will enhance the cost effectiveness of treatment.

8.4 Failure to attend for treatment
Patients who miss appointments for dosing should be managed according to the procedures in section 7.1 (page 62).

Patients who miss dosing appointments for seven or more consecutive days should be considered to have withdrawn from the opioid treatment program.

8.5 Involuntary withdrawal
At the beginning of treatment, patients sign a treatment agreement that specifies the conditions under which they may be involuntarily discharged. Situations that may warrant this action include:

Further information
• violence or threat of violence against staff or other patients
• property damage or theft from the clinic or dosing location
• drug dealing on or near the clinic or dosing location
• diversion of doses
• unacceptable disruption to the local amenity.

In some cases, transferring the patient to a different opioid replacement therapy may solve the problem without withdrawing treatment. Or it may be appropriate to transfer the patient to another service provider. If no options remain, methadone or buprenorphine treatment is withdrawn without the patient’s agreement. In this case, dose reduction should be gradual. Rapid dose reduction or abrupt cessation of treatment is warranted only in cases of violence, assault or threatened assault.

In the correctional setting, diversion of buprenorphine is not uncommon and is often related to a patient being “stood over” by another inmate. It is important that any contributing factors such as this are considered and that the patient is offered a transfer to methadone treatment rather than just having buprenorphine withdrawn.

8.5.1 Involuntary withdrawal from methadone

• Reduce dose by 10 mg per week until dose reaches 40 mg/day.
• Treatment can be ended at this point, or further reductions can be continued if circumstances permit.
• More abrupt termination of treatment is only acceptable to prevent violence.

8.5.2 Involuntary withdrawal from buprenorphine

• Reduce dose by 4 mg per week until dose reaches 4 mg/day.
• Treatment can be ended at this point, or further reductions can be continued if circumstances permit.
• More abrupt termination of treatment is only acceptable to prevent violence.

Advising the patient who is to be discharged of other treatment options, including detoxification. Warn the patient of the increased risk of overdose after completion of withdrawal. Assist the patient to reduce risks associated with resuming drug use and offer training in strategies to prevent relapse. Develop a management plan regarding subsequent readmission for each patient involuntarily withdrawn from the program and document it in the patient’s case record.

8.5.3 Complaints mechanism

All patients should have access to procedures for response to conflicts between themselves and their treatment providers.

All patients should have a fair opportunity to present their case. If possible, patients should be retained in the current treatment program pending the resolution of the complaint. See Appendix T (page 173) for an example of Area Health Service guidelines for involuntary discharge and a process for complaints.

8.6 Exiting and transferring patients

8.6.1 Treatment exit form

When a patient exits an opioid treatment program, or transfers between prescribers, a treatment exit form (available from the Pharmaceutical Services Branch [PSB]) must be completed and must be immediately forwarded to the PSB. Patients must be exited from treatment with one prescriber to begin treatment with another. This prevents patients being registered in two programs simultaneously and therefore being double-dosed.

8.6.2 Transfer of dosing site

If a patient has not changed prescriber but is to transfer between dosing sites, the PSB is to be notified by phone immediately of the change.

To avoid the potential for double dosing, the prescriber should notify the previous dosing site and have them cancel all scripts.

8.6.3 Transfer of information to new service provider

Where possible, and with the patient’s consent, information about the patient should be made available to the receiving clinical service. If patient consent is not given, disclosing information to another person or organisation involved in the ongoing care of the patient is possible, provided appropriate attention to confidentiality of this information is maintained.
If a service provider lacks information about the previous treatment of a new patient and initial assessment raises concerns about potential violence, he or she should contact the previous prescriber to determine the potential risk. The PSB (phone [02] 9879 5246) can be contacted to find the name of the previous prescriber.

It is appropriate to delay the start of treatment until all the necessary information is available to make an informed decision about suitability for treatment.

8.6.4 Refusal to exit a patient

No prescriber may refuse to complete exit procedures for a patient. Such an action would place the prescriber in breach of a condition of the authority to prescribe methadone or buprenorphine.

Refusing to exit patients has occurred in the past when money is owed to the service at which the patient has been dosed. A service in this position may pursue such civil remedies as are open to them to recover the debt. However, the patient must still be promptly exited to ensure further treatment is not blocked.

Persistent failure to exit patients may result in a review of approval to prescribe and where relevant, review of a clinic’s licence.

For information about temporary transfers of a patient for travel purposes, see section 7.27 on page 81.
Legal and administrative requirements

9.3 Approval to prescribe methadone and buprenorphine is granted by the Director-General of the NSW Department of Health.

9.6 Medical practitioners and drug and alcohol nurse practitioners are required to successfully complete:
- the Pharmacotherapy Accreditation Course for medical practitioners, either through attendance at a workshop or through the web-based course
- an examination
- a workplace assessment (a 2–3 hour clinical placement), or alternatively a written clinical case discussion that is assessed as satisfactory.

9.6 The Pharmacotherapy Credentialling Subcommittee assesses these requirements and the professional record of the prescriber.

9.7 Initially prescribers are granted approval to treat up to 25 patients with methadone or buprenorphine. An approved prescriber may, after a period of six months, apply for an increase in patient numbers.

9.8 Prescribers who are going on leave must arrange for a locum. A locum will ideally be experienced in the management of drug dependent patients. If possible, the locum should be an approved methadone and buprenorphine prescribing doctor or nurse practitioner.

9.9 All locum arrangements should be notified to the Pharmaceutical Services Branch (PSB).

9.10 If an authorised prescriber is unavailable 10 working days or less, locums should continue treatment in accord with the treatment plan, and the patient should be promptly reviewed by the authorised prescriber on their return to work. If an authorised prescriber is unavailable for more than 10 working days, the locum must accept responsibility for and be able to make all decisions relevant to patient care.

9.11 If the locum is an authorised prescriber, he or she should not accept responsibility for more than 50% above their authorised number of patients, and for not more than 250 patients in total, so that the quality of patient care is not compromised. While managing patients above their authorised number, authorised prescribers cannot enter new patients into treatment.

9.12 Clinics that provide opioid treatment are required to maintain accreditation according to NSW Health standards.

9.13 A prescriber must obtain authority to prescribe for each patient by completing an Application for authority to prescribe methadone/buprenorphine form and faxing it to the PSB of the NSW Department of Health (fax: [02] 9859 5170).

9.14 A patient must not begin methadone or buprenorphine treatment until approval has been given by PSB.

9.15 Increasing the dose beyond the authorised maximum requires a further application to and approval from the PSB.

9.16 An authority to prescribe is valid for a maximum of one year.

9.17 The Exit for Methadone and Buprenorphine Treatment form, also available from the PSB, must be completed and faxed to the PSB for each patient discharged from a program or transferred from the care of one prescriber to another.

9.18 Prescribers must comply with reporting requirements of the NSW Department of Health as a condition of authority to prescribe.

9.19 Methadone and buprenorphine prescriptions must be written in accordance with the requirements for drugs of addiction (Schedule 8) prescriptions set down under the Poisons and Therapeutic Goods Act 1966 (NSW). The prescriptions should not be handed to patients. They should be sent directly to the dispensing point to avoid any risk of alteration.
All stocks of methadone and buprenorphine must be stored in a manner approved by the PSB of the NSW Department of Health. Records must be maintained in good order in a drug register, showing all doses given each day and the balance at the end of the day.

Although it is the prescriber who determines the course of methadone or buprenorphine treatment, the dispenser is legally required to assess whether a dose of opioid is appropriate and can withhold treatment if considered necessary (eg, if the patient is intoxicated).

Pharmacists and nurses administering methadone or buprenorphine are not to increase the dose prescribed for a patient unless this is authorised by the prescriber on the prescription. They may have to decrease the dose administered — for example, if the patient has missed two or more doses or has used other psychoactive substances. The prescriber must be notified as soon as possible. If the conditions requiring a reduced dose are repeated on the next day, decreased dosage may again be necessary, even if the pharmacist or nurse has been unable to contact the prescriber. The safety of the patient is of paramount importance.
9.1 Legal and administrative framework for the Opioid Treatment Program

9.1.1 The Commonwealth Government Department of Health and Ageing:

- supplies methadone and buprenorphine to the dosing points (free of charge)
- pays for services by doctors (Medicare)
- approves the formulation and registration of products by way of the Therapeutic Goods Administration, which is also responsible for recall of faulty products
- prepares national policies and guidelines on the use of methadone and buprenorphine
- prepares national policies and guidelines on training
- tracks the use of narcotics.

9.1.2 The NSW State Government

9.1.2.1 Enabling legislation

The Poisons and Therapeutic Goods Act 1966 (NSW) and Regulations (2002) provide for:

- the authorisation of medical practitioners and nurse practitioners as prescribers of opioid treatments
- the review, amendment, and cancellation of medical practitioners’ or nurse practitioners’ authorities to prescribe
- procedures to allow patients who have been diagnosed as drug dependent to have access to treatment
- the licensing of private clinics
- the investigation of complaints regarding prescribing and the professional behaviour of prescribers
- regulation of the labelling, packing, storage, prescription and supply of products
- record-keeping on the use of drugs of addiction.

9.1.2.2 Mental Health and Drug & Alcohol Office (MHDAO):

- is the NSW Department of Health policy and administrative unit for drug and alcohol services
- undertakes statewide planning for service development
- promulgates clinical guidelines for the Opioid Treatment Program
- formulates policies to assist in the recruitment of pharmacy dosing points
- develops accreditation standards for opioid treatment clinics
- oversees the accreditation of clinics
- develops policies for the improved care of incarcerated patients and their continuity of care post-release
- liaises with local councils, police and community groups to handle issues of amenity in the vicinity of public and private clinics
- organises training for medical practitioners / nurse practitioners and accreditation of prescribers
- supports the Pharmacotherapy Credentialling Subcommittee, which provides expert clinical advice to the Director-General of the Department regarding authorisation, review and conditions on the authorities of prescribers (for more information on the Pharmacotherapy Credentialling Subcommittee, see section 9.2 on page 94)
- supports a liaison committee involving the Methadone Advice and Complaints Service (MACS), the Health Care Complaints Commission, Justice Health and a consumer group to receive reports on complaints and requests for advice received by MACS and to plan proactive strategies to improve the service.

The MHDAO is served by other specialised committees, including the Drug Health Council and the Quality in Treatment Committee (QIT).

The Drug Health Council is a forum of drug and alcohol managers from the Area Health Services which meets to coordinate policy and service development on a statewide basis.

The QIT reports to the Health Council and the MHDAO on matters relating to improvements in clinical practice and quality of care. It consists of senior clinicians from the Area Health Services with representation from non-government organisations, nursing and allied health professionals.

9.1.2.3 Pharmaceutical Services Branch (PSB) of NSW Health:

- maintains the database of authorised prescribers, dosing points and patients
- issues authorities to allow patients to be treated
- issues licences for private clinics
- inspects clinics and community pharmacies
- liaises with the Commonwealth
- monitors the labelling, packing, storage, prescription and supply of products.
9.1.2.4 Justice Health:
- is responsible for methadone or buprenorphine treatment for the prison population and for arranging continuity of care after release.

9.1.2.5 The Health Care Complaints Commission:
- provides patient support
- investigates serious complaints involving professional conduct, prescribing and behaviour
- refers serious cases to NSW Health or the Medical Board.

9.1.2.6 The NSW Medical Board:
- registers medical practitioners
- undertakes the investigation of serious complaints and implements appropriate training and disciplinary procedures
- imposes conditions on registration.

9.1.2.7 The NSW Nurses and Midwives Board:
- registers nurses and authorises nurse practitioners
- undertakes the investigation of serious complaints and implements appropriate remedial interventions and disciplinary procedures
- imposes conditions on registration.

9.1.3 Other bodies

9.1.3.1 The Methadone Advice and Complaints Service (MACS):
- provides information to patients on access to prescribers
- provides information to prescribers on access to dosing points
- logs complaints and provides support to patients
- reports to the MHDAO to assist in the resolution of complaints and the development of proactive strategies to address problems of access and quality of care
- can be contacted on: 1800 642 428.

9.1.3.2 NSW Users and AIDS Association (NUAA):
- is a consumer advocacy group
- provides support and advice to patients and other interested parties
- liaises with the MHDAO, MACS, Health Care Complaints Commission and Justice Health to monitor consumer satisfaction and plan ways to improve the system
- can be contacted on: 1800 644 413.

9.1.3.3 The Coroner’s Court
- records and investigates unexpected deaths, including drug-related deaths
- refers matters to the Health Care Complaints Commission for further investigation if appropriate
- refers matters to NSW Health for consideration with a view to service improvement or further investigation if necessary.

9.2 The Pharmacotherapy Credentialling Subcommittee

The Pharmacotherapy Credentialling Subcommittee is a subcommittee of the Medical Committee of NSW Health and is established under Section 30A of the Poisons and Therapeutic Goods Act 1966 (NSW). The primary role of the Pharmacotherapy Credentialling Subcommittee is to make recommendations to the Director-General on the approval of medical practitioners and nurse practitioners as prescribers of drugs of addiction under the State's Opioid Treatment Program.

9.3 Accreditation of prescribing doctors

Approval to prescribe methadone and buprenorphine is granted by the Director-General of the NSW Department of Health.

Medical practitioners (and nurse practitioners) are required to successfully complete:
- the Pharmacotherapy Accreditation Course, either through attendance at a workshop or through the web-based course
- an examination
- a workplace assessment (a 2–3 hour clinical placement).

These requirements and the professional record of the practitioner are assessed by the Pharmacotherapy Credentialling Subcommittee.

9.4 Authorisation to prescribe buprenorphine–naloxone

During the introduction of buprenorphine–naloxone treatment, a separate approval will be required for existing opioid treatment program prescribers to become authorised to prescribe buprenorphine–naloxone.

To gain such authorisation in NSW, doctors will need to:
- be experienced prescribers of methadone and/or buprenorphine. In practice, this means being a Fellow of the Chapter of Addiction Medicine, or managing patients in an opioid treatment program for at least 12
months, or working in recognised training posts under the supervision of experienced prescribers.

- satisfactorily complete a training module on the use of buprenorphine–naloxone. The course will be a four hour interactive case based training module, to be run by the Chapter of Addiction Medicine.

For existing accredited prescribers and non-accredited prescribers who prescribe to fewer than five patients, authority to prescribe buprenorphine–naloxone to a stable patient to whom they already prescribe buprenorphine may be granted (without completing the training module) on a patient by patient basis, by obtaining a supportive review from a specialist nominated by their Area Health Service.

9.5 Accreditation of prescribing nurse practitioners

Approval to prescribe methadone and buprenorphine is granted by the Director-General of the NSW Department of Health.

9.5.1 The nurse practitioner authorisation process

- Nurse practitioners in NSW undergo thorough authorisation processes through the NSW Nurses and Midwives Board.

- Applicants may either graduate from a Board-approved master’s degree program or provide evidence of their educational development and present to a clinical viva examination.

- Five thousand hours of practice at an advanced level in the identified specialty must be verified.

- Re-authorisation for all nurse practitioners is required every five years.

9.5.2 Nurse practitioners as opioid treatment prescribers

The additional training and credentialling requirements for drug and alcohol nurse practitioners to become prescribers of opioid pharmacotherapies are identical to those required of medical officers (see section 9.3, Accreditation of prescribing doctors, on page 94).

9.6 Limits on the number of patients able to be treated

During 2006 a review of the functions and operations of the Pharmacotherapy Credentialling Subcommittee was conducted. At this time the draft recommendations indicate that prescribers are no longer required to apply to the Pharmacotherapy Credentialling Subcommittee regarding an increase in patient numbers, instead the structure will be replaced by a system of increased monitoring depending upon the number of patients a prescriber chooses to manage. For information regarding an increase in patient numbers, contact the Secretary, Pharmacotherapy Credentialling Subcommittee, MHDAO, on (02) 9424 5791.

9.7 Locums

Prescribers who are going on leave and will not be available to their patients on methadone or buprenorphine must arrange for a locum prescriber. A locum will ideally be experienced in the management of drug dependent patients. If possible, the locum should be an approved methadone and buprenorphine prescriber.

All locum arrangements should be notified to the PSB (fax. [02] 9859 5170). In the case of retirement or planned leave for more than two weeks, the PSB should be notified beforehand of the proposed arrangements.

Locums should continue treatment according to the treatment plan, and the patient should be promptly reviewed by the authorised prescriber on their return to work. Changes to the patient treatment plan, such as prescribing benzodiazepines or increasing the frequency of regular takeaway doses, should not be initiated during short-term locum cover. Dose changes or prescription renewals should be written as short-term prescriptions valid only until the return of the authorised prescriber. Repeat locum prescriptions to cover brief periods of absence are not acceptable.

If an authorised prescriber is unavailable for more than 10 working days, the locum must accept responsibility for and be able to make all decisions relevant to patient care (including dose changes, provision of takeaway doses, management of concomitant conditions, dispensing point changes and transfers). Ideally, the locum will be an authorised pre-
scriber, and in this case the locum should ensure that he or she has not accepted responsibility for more than 50% above his or her authorised number of patients, and for not more than 250 patients in total, so that the quality of patient care is not compromised.

It is recognised that there will always be emergency situations and, if there is no other practitioner in the practice who is authorised to prescribe pharmacotherapies for opioid dependence, it is appropriate for another general practitioner who is in the practice and has access to the patient notes to write a script to cover the period during which the prescriber will be away, with no change in dose or takeaway doses. It is recommended that the duration of the script so written should not exceed one month.

9.7.1 Supernumerary places

In situations where transfer of care to another prescriber involves that prescriber in managing more than their authorised number of patients, the prescriber may be given supernumerary places, but will not be able to enter new patients into treatment until their number of patients falls below their approved number.

9.7.2 Retiring from prescribing

Prescribers intending to retire should write to the PSB and MHDAGO indicating their proposed retirement date (the date on which they relinquish their authority to prescribe) and arrangements for the ongoing care of their patients.

9.8 Accreditation of clinics

An important quality assurance and improvement mechanism is accreditation of services against agreed standards. Services that hold a licence to supply buprenorphine or methadone under the Poisons and Therapeutics Goods Act 1966 (NSW) are, as a condition of their licence, required to achieve accreditation and maintain accredited status with an approved organisation. Methadone and buprenorphine clinics operated by Area Health Services are required by the Director-General, NSW Department of Health, to achieve accreditation in accordance with the requirements placed on private licensed services. The NSW Methadone Clinic Accreditation Standards will be updated to apply to buprenorphine and methadone.

9.9 Authorisation to treat individual patients

The PSB administers the Poisons and Therapeutic Goods Act 1966 (NSW) and Poisons and Therapeutic Goods Regulation 2002 (NSW) and is responsible for issuing the authority to approved prescribers to treat individual patients with methadone or buprenorphine.

- A prescriber must obtain authority for each patient by completing an application for authority to prescribe [methadone/buprenorphine] form and faxing it to the PSB of the NSW Department of Health Fax. (02) 9859 5170.
- A patient must not begin methadone or buprenorphine treatment until approval has been given by the PSB. Approval may be checked by calling (02) 9879 5246.
- Increasing the dose beyond the authorised maximum requires a further application to and approval from the PSB.
- An authority to prescribe is valid for a maximum of one year.
- The Exit from methadone and buprenorphine treatment form, also available from the PSB, must be completed and faxed to PSB for each patient discharged from a program or transferred from the care of one prescriber to another.

Medical practitioners should be aware that Clause 79 of the Poisons and Therapeutic Goods Regulation 2002 (NSW) states that it is offence to prescribe a drug of addiction “in a quantity or for a purpose that does not accord with the recognised therapeutic standard of what is appropriate in the circumstances.”

9.10 Data collection and reporting

Accurate data are required to monitor treatment of opioid dependence with methadone and buprenorphine. Prescribers must comply with reporting requirements of the NSW Department of Health as a condition of authority to prescribe. This includes providing full details on the application for authority to prescribe, prompt submission of any changes in these details and prompt notification of treatment cessation.

The Brief treatment outcome measure — concise (BTOM-C) was developed for public clinics to administer, but it is no longer a mandatory requirement. For clinics that wish to continue using the measure, further information can be found below.

Further information

9.11 Prescriptions

Methadone and buprenorphine prescriptions must be written in accordance with the requirements for drugs of addiction (Schedule 8) prescriptions set down under the Poisons and Therapeutic Goods Act 1966 (NSW). The prescriptions should not be handed to patients. They should be sent directly to the dispensing point to avoid any risk of alteration.

9.12 Storage and administration of drugs

All stocks of methadone and buprenorphine must be stored in a manner approved by the PSB. Records must be maintained in good order in a drug register, showing all doses given each day and the balance at the end of the day. Entries are to be made in the drug register on the day the pharmacist or clinic receives, dispenses or administers methadone or buprenorphine.

Nurses, pharmacists and medical practitioners are able to administer methadone or buprenorphine to a patient, but only a pharmacist, an assistant under the direct supervision of a pharmacist, or a medical practitioner can dispense methadone or buprenorphine takeaway doses.

9.13 Control of dosing

Although it is the prescriber who determines the course of methadone or buprenorphine treatment, the dispenser is legally required to assess whether a dose of opioid is appropriate and can withhold treatment if considered necessary (eg, if the patient is intoxicated).

Patients are to be correctly identified before dosing.

The administering nurse, pharmacist or doctor must accurately measure the prescribed daily dose. Except in the case of takeaway doses, the dose is to be consumed by the patient under the direct supervision of the nurse, pharmacist or doctor, who is to ensure that methadone syrup is swallowed and that buprenorphine tablets are absorbed sublingually before the patient leaves.

Pharmacists and nurses administering methadone or buprenorphine are not to increase the dose prescribed for a patient unless this is authorised by the prescriber on the prescription and, in the case of clinics, also documented in the clinic’s policies and procedures.

Dispensing staff may have to decrease the dose administered from time to time. This is to be done only when necessary — for example, the patient has missed three or more doses or has used other psychoactive substances. The decrease in dosage will apply only on the occasion that made this change necessary. The prescriber must be notified as soon as possible and a permanent change of dosage should be discussed if necessary.

If the conditions requiring a reduced dose are repeated on the next day, reduced dosing may again be necessary, even if the pharmacist or nurse has been unable to contact the prescriber. The safety of the patient is of paramount importance.

However, all alterations in dose are to be discussed with the prescriber, who must approve any ongoing alterations. The exception to this may be when a clinic has clearly documented policies and procedures approved by the prescriber to deal with dose alterations. The prescriber remains ultimately responsible for all dose alterations.

No other changes may be made to the dose without instructions from the prescriber.

9.14 Other requirements for handling methadone

Excess methadone cannot be disposed of except under the supervision of an officer of the PSB or a Police Officer.

Labels on empty methadone syrup bottles should be defaced before discarding them and the bottles should be rinsed.
# 10 Appendices

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Opioid withdrawal rating scales</td>
<td>100</td>
</tr>
<tr>
<td>B</td>
<td>Methadone Syrup product information</td>
<td>104</td>
</tr>
<tr>
<td>C</td>
<td>Biodone Forte product information</td>
<td>107</td>
</tr>
<tr>
<td>D</td>
<td>Possible drug interactions with methadone</td>
<td>111</td>
</tr>
<tr>
<td>E</td>
<td>Buprenorphine product information</td>
<td>114</td>
</tr>
<tr>
<td>F</td>
<td>Buprenorphine–naloxone product information</td>
<td>120</td>
</tr>
<tr>
<td>G</td>
<td>Possible drug interactions with buprenorphine or buprenorphine–naloxone</td>
<td>127</td>
</tr>
<tr>
<td>H</td>
<td>Routine screening for domestic violence</td>
<td>128</td>
</tr>
<tr>
<td>I</td>
<td>Intoxication and withdrawal states from commonly used drugs</td>
<td>132</td>
</tr>
<tr>
<td>J</td>
<td>Assessment module for opioid treatment program induction</td>
<td>134</td>
</tr>
<tr>
<td>K</td>
<td>Example of written patient information for induction to treatment</td>
<td>145</td>
</tr>
<tr>
<td>L</td>
<td>Suitability for takeaway doses assessment form</td>
<td>148</td>
</tr>
<tr>
<td>M</td>
<td>NSW Health forms used in the administration of the Opioid Treatment Program</td>
<td>150</td>
</tr>
<tr>
<td>N</td>
<td>Example of a formal warning letter</td>
<td>164</td>
</tr>
<tr>
<td>O</td>
<td>Patient identification</td>
<td>165</td>
</tr>
<tr>
<td>P</td>
<td>Managing attempted buprenorphine diversion</td>
<td>166</td>
</tr>
<tr>
<td>Q</td>
<td>Drugs of addiction (Schedule 8 of the NSW Poisons List)</td>
<td>169</td>
</tr>
<tr>
<td>R</td>
<td>Patient consent form for buprenorphine treatment during pregnancy or breastfeeding</td>
<td>170</td>
</tr>
<tr>
<td>S</td>
<td>Neonatal withdrawal scoring chart</td>
<td>171</td>
</tr>
<tr>
<td>T</td>
<td>Guidelines for involuntary discharge</td>
<td>173</td>
</tr>
<tr>
<td>U</td>
<td>Acknowledgements</td>
<td>174</td>
</tr>
<tr>
<td>V</td>
<td>Guidelines and Information Sheets Regarding Suboxone® Sublingual Film</td>
<td>175</td>
</tr>
</tbody>
</table>
### Opioid withdrawal rating scales

<table>
<thead>
<tr>
<th>Scale</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Opiate Withdrawal Scale (COWS)</td>
<td>101</td>
</tr>
<tr>
<td>Subjective Opiate Withdrawal Scale (SOWS)</td>
<td>102</td>
</tr>
<tr>
<td>Objective Opioid Withdrawal Scale (OOWS)</td>
<td>103</td>
</tr>
</tbody>
</table>
### Clinical Opiate Withdrawal Scale (COWS)

For each item, circle the number that best describes the patient’s signs or symptom. Rate on just the apparent relationship to opiate withdrawal. For example, if heart rate is increased because the patient was jogging just prior to assessment, the increased pulse rate would not add to the score.

**Patient’s Name: __________________ Date and Time: ____/_____/____:______**

**Reason for this assessment: __________________________________________________**

<table>
<thead>
<tr>
<th>Resting Pulse Rate: ______ beats/minute</th>
<th>GI upset: over last ½ hour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measured after patient is sitting or lying for one minute</td>
<td>0 no GI symptoms</td>
</tr>
<tr>
<td>0 pulse rate 80 or below</td>
<td>1 stomach cramps</td>
</tr>
<tr>
<td>1 pulse rate 81–100</td>
<td>2 nausea or loose stool</td>
</tr>
<tr>
<td>2 pulse rate 101–120</td>
<td>3 vomiting or diarrhoea</td>
</tr>
<tr>
<td>4 pulse rate greater than 120</td>
<td>5 multiple episodes of diarrhoea or vomiting</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sweating: over past ½ hour not accounted for by room temperature or patient activity.</th>
<th>Tremor. Observation of outstretched hands</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 no report of chills or flushing</td>
<td>0 no tremor</td>
</tr>
<tr>
<td>1 subjective report of chills or flushing</td>
<td>1 tremor can be felt, but not observed</td>
</tr>
<tr>
<td>2 flushed or observable moistness on face</td>
<td>2 slight tremor observable</td>
</tr>
<tr>
<td>3 beads of sweat on brow or face</td>
<td>4 gross tremor or muscle twitching</td>
</tr>
<tr>
<td>4 sweat streaming off face</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Restlessness. Observation during assessment</th>
<th>Yawning. Observation during assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 able to sit still</td>
<td>0 no yawning</td>
</tr>
<tr>
<td>1 reports difficulty sitting still, but is able to do so</td>
<td>1 yawning once or twice during assessment</td>
</tr>
<tr>
<td>3 frequent shifting or extraneous movements of legs/arms</td>
<td>2 yawning three or more times during assessment</td>
</tr>
<tr>
<td>5 unable to sit still for more than a few seconds</td>
<td>4 yawning several times/minute</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pupil size</th>
<th>Anxiety or irritability</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 pupils pinned or normal size for room light</td>
<td>0 none</td>
</tr>
<tr>
<td>1 pupils possibly larger than normal for room light</td>
<td>1 patient reports increasing irritability or anxiousness</td>
</tr>
<tr>
<td>2 pupils moderately dilated</td>
<td>2 patient obviously irritable anxious</td>
</tr>
<tr>
<td>5 pupils so dilated that only the rim of the iris is visible</td>
<td>4 patient so irritable or anxious that participation in the assessment is difficult</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bone or joint aches. If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored</th>
<th>Gooseflesh skin</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 not present</td>
<td>0 skin is smooth</td>
</tr>
<tr>
<td>1 mild diffuse discomfort</td>
<td>3 piloerection of skin can be felt or hairs standing up on arms</td>
</tr>
<tr>
<td>2 patient reports severe diffuse aching of joints/muscles</td>
<td>5 prominent piloerection</td>
</tr>
<tr>
<td>4 patient is rubbing joints or muscles and is unable to sit still because of discomfort</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Runny nose or tearing not accounted for by cold symptoms or allergies</th>
<th>Total score</th>
<th>Initials of person completing assessment: ____________</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 not present</td>
<td>The total score is the sum of all 11 items</td>
<td></td>
</tr>
<tr>
<td>1 nasal stuffiness or unusually moist eyes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 nose running or tearing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 nose constantly running or tears streaming down cheeks</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Score: 5–12 = mild; 13–24 = moderate; 25–36 = moderately severe; more than 36 = severe withdrawal.
Subjective Opiate Withdrawal Scale (SOWS)

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
<th>Please score each of the 16 items below according to how you feel NOW (circle one number)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td><strong>Symptom</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Not at all</strong>  <strong>A little</strong>  <strong>Moderately</strong>  <strong>Quite a bit</strong>  <strong>Extremely</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 I feel anxious</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 I feel like yawning</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 I am perspiring</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 My eyes are teary</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5 My nose is running</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6 I have goosebumps</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7 I am shaking</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8 I have hot flushes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>9 I have cold flushes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10 My bones and muscles ache</td>
</tr>
<tr>
<td></td>
<td></td>
<td>11 I feel restless</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12 I feel nauseous</td>
</tr>
<tr>
<td></td>
<td></td>
<td>13 I feel like vomiting</td>
</tr>
<tr>
<td></td>
<td></td>
<td>14 My muscles twitch</td>
</tr>
<tr>
<td></td>
<td></td>
<td>15 I have stomach cramps</td>
</tr>
<tr>
<td></td>
<td></td>
<td>16 I feel like using now</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Range 0–64.</td>
</tr>
</tbody>
</table>

### Objective Opioid Withdrawal Scale (OOWS)

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
<th>Objective Opioid Withdrawal Scale (OOWS)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Observe the patient for 5 minutes, then indicate a score for each of the opioid withdrawal signs listed below. Add the scores for each item to obtain the total score.</td>
</tr>
<tr>
<td>1</td>
<td>Yawning</td>
<td>0 = no yawning 1 = yawning</td>
</tr>
<tr>
<td>2</td>
<td>Rhinorrhoea</td>
<td>0 &lt; 3 sniffs 1 = 3 or more sniffs</td>
</tr>
<tr>
<td>3</td>
<td>Piloerection (observe arm)</td>
<td>0 = absent 1 = present</td>
</tr>
<tr>
<td>4</td>
<td>Perspiration</td>
<td>0 = absent 1 = present</td>
</tr>
<tr>
<td>5</td>
<td>Lacrimation</td>
<td>0 = absent 1 = present</td>
</tr>
<tr>
<td>6</td>
<td>Tremor (hands)</td>
<td>0 = absent 1 = present</td>
</tr>
<tr>
<td>7</td>
<td>Mydriasis</td>
<td>0 = absent 1 = ≥ 3 mm</td>
</tr>
<tr>
<td>8</td>
<td>Hot and cold flushes</td>
<td>0 = absent 1 = shivering / huddling for warmth</td>
</tr>
<tr>
<td>9</td>
<td>Restlessness</td>
<td>0 = absent 1 = frequent shifts of position</td>
</tr>
<tr>
<td>10</td>
<td>Vomiting</td>
<td>0 = absent 1 = present</td>
</tr>
<tr>
<td>11</td>
<td>Muscle twitches</td>
<td>0 = absent 1 = present</td>
</tr>
<tr>
<td>12</td>
<td>Abdominal cramps</td>
<td>0 = absent 1 = holding stomach</td>
</tr>
<tr>
<td>13</td>
<td>Anxiety</td>
<td>0 = absent 1 = mild to severe</td>
</tr>
</tbody>
</table>

**Total score**

Range 0–3.

B Methadone Syrup product information

This product information was supplied by the manufacturer, GlaxoSmithKline, in August 2004, and may have been updated since that time. For the most recent product information, check with GlaxoSmithKline <www.gsk.com.au>

NAME OF THE DRUG: Methadone hydrochloride

DESCRIPTION

C_{21}H_{27}NO\cdot HCl = 345.9

Methadone hydrochloride is a synthetic opioid analgesic with the general properties of morphine. Methadone is a racemic mixture and levo-methadone is the active isomer.

It occurs as odourless, colourless crystals or white crystalline powder. It is soluble in water, freely soluble in alcohol and chloroform; practically insoluble in ether and in glycerol.

PHARMACOLOGY

The pharmacological actions of methadone are qualitatively similar to those of morphine. Significant quantitative differences are its effective analgesic activity after administration by the oral route and its tendency to show persistent effects with repeated administration.

Methadone hydrochloride is readily absorbed after administration by mouth and has high oral bioavailability. Peak plasma concentrations have been reported 1 to 5 hours after oral administration of a single dose in tablet form. It undergoes considerable tissue distribution and protein binding is reported to be 60% to 90% with α₁-acid glycoprotein being the main binding protein in plasma. Metabolism to the major metabolite 2-ethylidine-1,5-dimethyl-3,3-diphenylpyrrolidine and the minor metabolite 2-ethyl-3,3-diphenyl-5-methylpyrrolidine, both of them inactive, occurs in the liver. These metabolites are excreted in the faeces and urine together with unchanged methadone. Other metabolites, including methadol and normethadol (reported to be pharmacologically active), have also been described but account for a small proportion of the dose. The liver may also serve as a major storage site of unchanged methadone, which is taken up, bound nonspecifically by the liver and released again mainly unchanged.

Marked individual variations in kinetics have been observed with methadone. Elimination half-lives vary considerably (a range of 15 to 60 hours has been reported) and careful adjustment of dosage is necessary with repeated administration.

Plasma concentrations have been found to vary widely during methadone maintenance therapy, with large differences between patients and wide fluctuations in individual patients. Declining concentrations have been reported during methadone maintenance suggesting that tolerance occurs, possibly as a result of auto-induction of hepatic microsomal enzymes.

INDICATIONS

Methadone Syrup is indicated for the treatment of dependence on opioid drugs.

CONTRAINDICATIONS

Methadone Syrup is contraindicated in individuals who are hypersensitive to methadone or other components in Methadone Syrup.

Like other opioids, methadone is contraindicated in patients with respiratory depression, especially in the presence of cyanosis and excessive bronchial secretions.

Methadone should not be given during an attack of bronchial asthma.

Methadone is contraindicated in the presence of acute alcoholism, head injury and raised intracranial pressure.

Methadone is contraindicated in individuals receiving monoamine oxidase inhibitors or within 14 days of stopping such treatment.

As with other opioids, methadone is contraindicated in patients with ulcerative colitis, since it may precipitate toxic dilation or spasm of the colon.

As with all narcotic analgesics, methadone should not be administered to patients with severe hepatic impairment as it may precipitate hepatic encephalopathy (see PRECAUTIONS).

Methadone is contraindicated in biliary and renal tract spasm.

PRECAUTIONS

In common with all opioids, prolonged use of methadone has the potential to produce dependence of the morphine type.

Methadone should be used with caution in the presence of hypothyroidism, adrenocortical insufficiency, hypopituitarism, prostatic hypertrophy, shock, and diabetes mellitus.

Extreme caution should be exercised when administering methadone to patients with phaeochromocytoma, since aggravated hypertension has been reported in association with diamorphine.

In common with other opioids, methadone may produce orthostatic hypotension and drowsiness in ambulatory patients. They should be cautioned, therefore, against driv-
Clinical guidelines for methadone and buprenorphine treatment of opioid dependence

ING VEHICLES, OPERATING MACHINERY OR OTHER ACTIVITIES REQUIRING VIGILANCE.

METHADONE SYRUP IS NOT SUITABLE FOR ADMINISTRATION BY INJECTION.

METHADONE SYRUP IS FOR ORAL USE ONLY.

MUTAGENIC POTENTIAL

Methadone did not exhibit demonstrable mutagenic activity in a wide range of standard in vitro and in vivo mutagenicity assays. However, in a Dominant Lethal assay in mice, treatment with methadone at doses between 1 and 6 mg/kg was associated with increased pre-implantation deaths and chromosomal aberrations of sperm cells when compared with controls.

CARCINOGENIC POTENTIAL

Long-term carcinogenicity tests in rodents did not reveal any evidence of methadone-related neoplasia.

TERATOGENIC POTENTIAL

No teratogenic effects have been observed in standard teratogenicity studies in rats and rabbits given methadone at doses from 10 to 50 times the average daily human maintenance dose. Developmental abnormalities of the central nervous system have been reported in hamsters and mice given high doses in early pregnancy.

FERTILITY

Methadone does not appear to impair human female fertility.

Studies in men on methadone maintenance programs have shown that methadone reduces serum testosterone and markedly depresses the ejaculate volume and sperm motility. The sperm counts of methadone subjects were twice that of controls but this reflected the lack of dilution from seminal secretions. A reduction in libido has been reported as well as impotence, delayed, and/or failed ejaculation.

USE IN PREGNANCY (CATEGORY C)

Narcotic analgesics may cause respiratory depression in the newborn infant. During the last 2-3 hours before expected delivery, narcotic analgesics should therefore only be used after weighing the needs of the mother against the risk to the fetus.

Withdrawal symptoms may be observed in infants born to mothers receiving methadone maintenance consisting of central nervous system, gastrointestinal, and respiratory disturbances.

Infants born to mothers on methadone maintenance have been reported to have smaller birth weights when compared to infants of non-drug exposed mothers. The infants born to mothers on methadone maintenance were not small for gestational age, and by six months of age, these infants did not exhibit any general development sequelae.

USE IN LACTATION

Breastfeeding is permissible in mothers receiving methadone for maintenance therapy but the baby should be monitored to avoid sedation. Withdrawal symptoms can occur in the infant. Assays of breast milk from methadone maintained mothers showed methadone concentrations of 0.17 to 5.6 μg/mL.

INTERACTIONS WITH OTHER DRUGS

Monoamine oxidase inhibitors (MAOIs) may prolong and enhance the respiratory depressant effects of methadone. Opioids and MAOIs used together may cause fatal hypotension and coma.

Rifampicin has been reported to reduce circulating levels of methadone and increase its urinary excretion in these patients. The resulting lowered plasma concentrations of methadone induced withdrawal symptoms.

Phenytoin has been reported to enhance the metabolism of methadone with resulting withdrawal symptoms in the patients.

Patients on methadone maintenance who are also taking enzyme inducers such as carbamazepine may require higher than typical doses of methadone.

The general depressant effects of methadone may be enhanced by other centrally acting agents such as alcohol, barbiturates, neuromuscular blocking agents, phenothiazines and tranquilisers. Some psychotropic drugs, however, may potentiate the analgesic effects of methadone.

Propranolol has been reported to enhance the lethality of toxic doses of opioids in animals. Although the significance of this finding is not known for man, caution should be exercised when such drugs are co-administered.

USE IN CHILDREN

Methadone is not recommended for use in children less than 18 years of age since documented clinical experience has been insufficient to establish a suitable dosage regimen; furthermore, children are particularly sensitive to the respiratory and central nervous system effects of methadone.

USE IN THE ELDERLY

Methadone has a long plasma half-life, which may lead to accumulation, particularly if renal function is impaired (see Renal impairment).

In common with other opioids, methadone may cause confusion in this age group, therefore careful monitoring is advised.

HEPATIC IMPAIRMENT

Particular care should be taken when methadone is to be used in patients with hepatic impairment as these patients...
metabolise methadone more slowly than normal patients. Where not contraindicated, methadone should be given at less than the normal recommended dose and the patient’s response used as a guide to further dosage requirements (see CONTRAINDICATIONS).

Renal impairment

Methadone should be used with caution in patients with renal dysfunction.

ADVERSE REACTIONS

Respiratory

The major side effect of methadone is respiratory depression.

Gastrointestinal

Reported events include nausea, vomiting, and dry mouth. Methadone, in common with other opioids may cause spasm of the biliary tract (see CONTRAINDICATIONS).

Neurological

Reported events include dizziness*, drowsiness*, light-headedness*, sweating* and confusion*. Euphoria has been reported at higher doses in tolerant patients.

* These adverse reactions appear to be more common in ambulatory patients and in those receiving oral therapy.

Cardiovascular

Hypotension, collapse, and generalised oedema have occasionally been reported.

Renal

Methadone, in common with other opioids may cause spasm of the renal tract (see CONTRAINDICATIONS). It also possesses antiuretic properties.

Endocrine

Prolonged use of methadone in men has been reported to be associated with the development of gynaecomastia.

DOSAGE AND ADMINISTRATION

A dose of 10 to 20 mg by mouth may be given initially and increased as necessary by 5 to 10 mg daily. The dose must not be increased by more than 5 to 10 mg daily, and by no more than 30 mg in any seven-day period. After stabilisation, which can often be achieved with a daily dose of 30 to 50 mg daily (up to a maximum of 80 mg daily), the dose of methadone is gradually decreased until total withdrawal is achieved. Some treatment schedules for opioid dependence involved prolonged maintenance therapy with methadone where the daily dose is adjusted carefully for the individual.

OVERDOSAGE

Symptoms and signs

The symptoms and signs of overdosage with methadone parallel those for other opioids, namely profound respiratory depression, pinpoint pupils, hypotension circulatory failure and pulmonary oedema and coma.

Mydriasis may replace miosis as asphyxia intervenes. Drowsiness, floppiness, pin-point pupils and apnoea have been reported in children.

Treatment

General supportive measures should be employed as required. The specific opioid antagonist naloxone can be used for the reversal of coma and the restoration of spontaneous respiration. Intravenous infusion is the preferred route of administration in the management of methadone overdose because of the short half-life of naloxone relative to the long half-life of methadone, continuous infusion reduces the possibility of prolonged respiratory depression and the risk of relapse, which can occur suddenly.

Patients should be monitored closely for at least 48 hours after apparent recovery in case of relapse, since the duration of action of the antagonist may be substantially shorter than that of methadone.

The use of other respiratory or central stimulants is not recommended.

Acidification of the urine will enhance urinary excretion of methadone.

Methadone is not dialysable by either peritoneal or haemodialysis.

Presentation

Oral liquid containing methadone hydrochloride 5 mg/mL.

Pack sizes: 200 mL, 1 litre.

Storage: Store below 25°C. Protect from light. Schedule: S8 in all states.

NAME AND ADDRESS OF THE SPONSOR

Glaxo Wellcome Australia Ltd A.C.N. 004 148 065
1061 Mountain Highway
Boronia Victoria 3155

Approved by the Therapeutic Goods Administration (TGA) on 17 June 1994.

Date of safety-related notification to the TGA: 12 September 1995.

Date of most recent amendment: 17 April 2000.
C Biodone Forte product information

This product information was supplied by the manufacturer, McGaw Biomed Pty Ltd, in July 2005, and may have been updated since that time. For the most recent product information, check with McGaw Biomed.

NAME OF THE DRUG

Methadone hydrochloride: (6-dimethylamino-4,4-diphenyl-3-heptanone hydrochloride).

C\textsubscript{21}H\textsubscript{27}NO.HCl MW = 345.9

CAS registry number 1095-90-5

Formula (Me = CH\textsubscript{3})

Methadone is a racemic mixture of two enantiomers. The $l$-enantiomer is more potent with respect to analgesic activity, respiratory depression and addiction liability.

DESCRIPTION

Methadone hydrochloride is a synthetic opioid analgesic with the general properties of morphine.

It occurs as odourless, colourless crystals or white crystalline powder. It is soluble in water, freely soluble in alcohol and chloroform, particularly insoluble in ether and in glycerol.

Biodone Forte is a solution of methadone hydrochloride in water. It also contains permicol red.

PHARMACOLOGY

The pharmacological actions of methadone are qualitatively similar to those of morphine. Significant quantitative differences are its effective analgesic activity after administration by the oral route and its tendency to show persistent effects with repeated administration.

Methadone hydrochloride is readily absorbed after administration by mouth and has high oral bioavailability. Peak plasma concentrations have been reported 1 to 5 hours after oral administration of a single dose in tablet form. It undergoes considerable tissue distribution and protein binding is reported to be 60 to 90% with $\alpha\_1$,-acid glycoprotein being the main binding protein in the plasma. Metabolism to the major metabolite 2-ethylidine-1,5-dimethyl, 3,3-diphenylpyrrolidine and the minor metabolite 2-ethyl-3,3-diphenyl-5-methylpyrrolidine, both of them inactive, occurs in the liver. These metabolites are excreted in the faeces and urine together with unchanged methadone. Other metabolites, including methadol and normethadol (reported to be pharmacologically active), have also been described but account for a small proportion of the dose. The liver may also serve as a major storage site of unchanged methadone which is taken up, bound non-specifically by the liver and released again mainly unchanged.

Marked interindividual variations in kinetics have been observed with methadone. Elimination half-lives vary considerably (a range of 15 to 60 hours has been reported) and careful adjustment of dosage is necessary with repeated administration, after which there is a gradual accumulation in the tissues.

Plasma concentrations have been found to vary widely during methadone maintenance therapy with large differences between patients and wide fluctuations in individual patients. Declining concentrations have been reported during methadone maintenance suggesting that tolerance occurs, possibly as a result of auto-induction of hepatic microsomal enzymes.

INDICATIONS

Biodone Forte is indicated for the detoxification and maintenance treatment of dependence on opioid drugs.

CONTRAINDICATIONS

Biodone Forte is contraindicated in individuals who are hypersensitive to methadone or permicol red, which are the only components in the formulation.

Like other opioids, methadone is contraindicated in patients with respiratory depression, especially in the presence of cyanosis and excessive bronchial secretions.

Methadone should not be given during an attack of bronchial asthma.

Methadone is contraindicated in the presence of acute alcoholism, head injury and raised intracranial pressure.

Methadone is contraindicated in individuals receiving monoamine oxidase inhibitors or within 14 days of stopping such treatment.

As with other opioids, methadone is contraindicated in patients with ulcerative colitis, since it may precipitate toxic dilation or spasm of the colon.

As with all opioid analgesics, methadone should not be administered to patients with severe hepatic impairment as it may precipitate hepatic encephalopathy (see PRECAUTIONS).

Methadone is contraindicated in biliary and renal tract spasm.

Methadone is contraindicated in individuals with existing QT prolongation, including those with congenital long QT syndrome (see PRECAUTIONS).

PRECAUTIONS

In common with all opioids, prolonged use of methadone has the potential to produce dependence of the morphine type.
The withdrawal symptoms are less intense but more prolonged than those produced by morphine or diamorphine. They develop more slowly and do not usually appear until 24 to 48 hours after the last dose. Discontinuation of methadone therapy should be carried out gradually in patients who may have developed physical dependence on the medicine so as to avoid precipitating withdrawal symptoms (see ADVERSE REACTIONS).

Methadone should be used with caution in the presence of hypothyroidism, adrenocortical insufficiency, hypopituitarism, prostatic hypertrophy, shock and diabetes mellitus.

Extreme caution should be exercised when administering methadone to patients with phaeochromocytoma, since aggravated hypertension has been reported in association with diamorphine.

In vivo and in vitro studies have demonstrated that methadone inhibits cardiac potassium channels and prolongs cardiac repolarisation (ie prolongs the QT interval). QT interval prolongation and serious arrhythmia (Torsade de pointes) have been observed during treatment with methadone and appear to be more common with higher doses. Particular caution and careful monitoring is recommended in patients at risk of prolonged QT interval (eg cardiac hypertrophy, concomitant diuretic use, hypokalaemia, hypomagnesia), patients with a previous history of cardiac repolarisation prolongation, those taking medications affecting cardiac repolarisation or methadone metabolism, and in patients with an increased risk of arrhythmia (see CONTRAINDICATIONS and Interactions with other drugs). Patients developing QT prolongation while on methadone treatment should be evaluated for modifiable risk factors, such as concomitant medications with cardiac effects, drugs which might cause electrolyte abnormalities, and drugs which might act as inhibitors of methadone metabolism.

**Biodone Forte is not intended for administration by injection.**

**Biodone Forte is for oral use only.**

**Carcinogenicity, mutagenicity and impairment of fertility**

Methadone did not exhibit demonstrable mutagenic activity in a wide range of standard in vitro and in vivo mutagenicity assays. However in a Dominant Lethal assay in mice treatment with methadone at doses between 1 and 6 mg/kg was associated with increased pre-implantation deaths and chromosomal aberrations of sperm cells when compared with controls.

Long-term carcinogenicity tests in rodents did not reveal any evidence of methadone related neoplasia.

Methadone does not appear to impair human female fertility.

Studies in men on methadone maintenance programs have shown that methadone reduces serum testosterone and markedly depresses the ejaculate volume and sperm motility. The sperm counts of methadone subjects were twice that of controls but this reflected the lack of dilution from seminal secretions. A reduction in libido has been reported as well as impotence, delayed and/or failed ejaculation.

**Use in pregnancy (Category C)**

There is insufficient evidence on which to determine the safety profile of methadone in pregnancy, therefore it should only be used if the potential benefit outweighs the potential risk.

No teratogenic effects have been observed in standard teratogenicity studies in rats and rabbits given methadone at doses from 10 to 50 times the average daily human maintenance dose. Developmental abnormalities of the central nervous system have been reported in hamsters and mice given high doses in early pregnancy.

Opioid analgesics may cause respiratory depression in the newborn infant. During the last 2–3 hours before expected delivery, opioid analgesics should therefore only be used after weighing the needs of the mother against the risk to the fetus. Methadone is not recommended for use during labour because its prolonged duration of action increases the risk of respiratory depression in the neonate.

Like other opioids, methadone crosses the placenta during pregnancy, and most neonates born to mothers on methadone maintenance will suffer from withdrawal if left untreated.

Withdrawal symptoms pertaining to the central nervous system, gastrointestinal system and respiratory system may be observed in infants born to mothers receiving methadone maintenance. Neonatal abstinence syndrome may not occur until some days after birth. Therefore, in addition to initial monitoring of respiratory depression, neonates should undergo prolonged monitoring for signs and symptoms of methadone withdrawal.

Infants born to mothers on methadone maintenance have been reported to have smaller birth weights when compared to infants of non-drug-exposed mothers. The infants born to mothers on methadone were not small for gestational age, and by six months of age, these infants did not exhibit any general development sequelae.

**Use in lactation**

Methadone is distributed into breast milk with a mean ratio of milk to plasma concentration of 0.44. However, doses of methadone to the infant by breast milk are low, estimated at 3% of maternal dose, on average, and insufficient to prevent neonatal abstinence syndrome in infants born to mothers on methadone maintenance.

Breastfeeding is permissible in mothers receiving methadone for maintenance therapy but the baby should be monitored to avoid sedation.

**Interactions with other drugs**

Methadone is metabolised by various cytochrome P450 (CYP450) enzymes. Therefore, coadministration of drugs known to interfere with the CYP450 enzymes may affect its clinical activity.

Some compounds may increase the metabolism of methadone (eg, rifampicin, phenytoin, carbamazepine, St John's Wort, and antiretroviral agents used in the treatment of HIV infection, par-
particularly nevirapine, efavirenz and some protease inhibitors). This has the potential to result in withdrawal symptoms.

Patients on methadone maintenance who are also taking enzyme inducers such as carbamazepine, may require higher than typical doses of methadone.

Some compounds may decrease the metabolism of methadone (eg, fluconazole and some serotonin re-uptake inhibitors [SSRIs], particularly fluvoxamine). This may increase the likelihood of toxicity.

In addition to compounds that may decrease the metabolism of methadone, extreme caution is necessary when any drug known to have the potential to prolong the QT interval is prescribed in conjunction with methadone (see PRECAUTIONS). Interactions may occur with methadone and potentially arrhythmogenic agents such as class I and III antiarrhythmics, some neuroleptics and tricyclic antidepressants, and calcium channel blockers. Caution should also be exercised when prescribing concomitant drugs capable of inducing electrolyte disturbances that may prolong the QT interval (hypokalaemia, hypomagnesaemia). These include diuretics, laxatives and in rare cases mineralocorticoid hormones.

Methadone can also affect the metabolism of other drugs. Plasma concentrations of some drugs may be increased (eg, neflaminav, zidovudine, fluconazole and desipramine), whereas concentrations of other drugs may be decreased, (eg, abacavir and amprenavir).

Monoamine oxidase inhibitors (MAOIs) may prolong and enhance the respiratory depressant effects of methadone. Opioids and MAOIs used together may cause fatal hypotension and coma.

The general depressant effects of methadone may be enhanced by other centrally-acting agents such as alcohol, barbiturates, neuromuscular blocking agents, phenothiazines and tranquillisers. Some psychotropic drugs, however, may potentiate the analgesic effects of methadone. The intestinal effects of methadone may delay the absorption of mexiletine.

Propranolol has been reported to enhance the lethality of toxic doses of opioids in animals. Although the significance of this finding is not known for man, caution should be exercised when such drugs are co-administered.

Opioid analgesics may antagonise the effects of agents that stimulate gastrointestinal motility (metoclopramide, domperidone, cisapride).

Anticholinergics increase the risk of constipation, urinary retention and so on. Antihypertensives may aggravate the hypotensive effects of opioid analgesics.

**Use in children**

Methadone is not recommended for use in children less than 18 years of age since documented clinical experience has been insufficient to establish a suitable dosage regimen, furthermore, children are particularly sensitive to the respiratory and central nervous system effects of methadone.

**Use in the elderly**

Methadone has a long plasma half-life, which may lead to accumulation, particularly if renal function is impaired (see Renal Impairment).

In common with other opioids, methadone may cause confusion in this age group, therefore careful monitoring is advised.

**Hepatic impairment**

Particular care should be taken when methadone is to be used in patients with hepatic impairment as these patients metabolise methadone more slowly than normal patients. Where not contraindicated, methadone should be given at less than the normal recommended dose and the patient’s response used as a guide to further dosage requirements (see CONTRAINDICATIONS).

**Renal impairment**

Methadone should be used with caution in patients with renal dysfunction.

**Cardiac repolarisation disorders**

Methadone should be administered with particular caution to patients at risk for development of prolonged QT interval (see PRECAUTIONS and CONTRAINDICATIONS).

**Effects on the ability to drive or operate machinery**

In common with other opioids methadone may produce orthostatic hypotension and drowsiness in ambulatory patients. They should be cautioned, therefore, against driving vehicles, operating machinery or other activities requiring vigilance.

**Effects on laboratory tests**

The serum BSP retention test may be increased (hepatotoxic effect or spasm of sphincter of Oddi). Plasma cortisol may be increased in response to cold to an extent not seen in controls. An increase in the serum albumin, prolactin and immunoglobulin IgG levels may be seen as a response to chronic administration. A significant decrease in serum indocyanine green level has been observed in a small series of patients with normal liver function tests. PCO₂ may be increased due to decreased pulmonary ventilation. False positive urine pregnancy tests have occurred, mainly with the Gravidx test. Physiological changes in thyroid hormones may be seen — decrease in serum thyroxine (T₄), a decrease in free thyroxine and an increase in tri-iodothyronine (T₃).

**ADVERSE REACTIONS**

The major side effect of methadone is respiratory depression.

Other reported events include nausea, vomiting, constipation, dizziness, drowsiness, light-headedness, dry mouth, sweating and confusion. These effects appear to be more common in ambulatory patients and in those receiving oral therapy. Less common reactions include bradycardia, tachycardia, palpitations, blurred vision, stomach cramps or pain.
Euphoria has been reported at higher doses in tolerant patients.

Hypotension, collapse, and generalised oedema have occasionally been reported. EEG changes including QT prolongation and torsades de pointes have occurred very rarely, usually in patients with risk factors or receiving high doses of methadone (see PRECAUTIONS).

Chronic use of opioid analgesics may be associated with the development of physical dependence. A withdrawal (abstinence) syndrome may be precipitated when opioid administration is suddenly discontinued or opioid antagonists administered. Withdrawal symptoms that may be observed after discontinuation of opioid use include body aches, diarrhoea, piloerection, anorexia, nervousness or restlessness, rhinorrhea, sneezing, tremors or shivering, abdominal colic, nausea, sleep disturbance, unusual increase in sweating or yawning, weakness, tachycardia and unexplained fever. With appropriate dose adjustment and gradual withdrawal these symptoms are usually mild.

Methadone, in common with other opioids may cause spasm of the biliary and renal tracts (see CONTRAINDICATIONS). It also possesses antidiuretic properties.

Prolonged use of methadone in men has been reported to be associated with the development of gynaecomastia.

DOSAGE AND ADMINISTRATION

Dosage and duration of treatment should be individualised.

A dose of 10 to 20 mg by mouth may be given initially and increased as necessary by 5 to 10 mg daily. The dose must not be increased by more than 5 to 10 mg daily, and by no more than 30 mg in any seven day period. After stabilisation, which can often be achieved with a daily dose of 30 to 50 mg daily (up to a maximum of 80 mg daily), the dose of methadone is gradually decreased until total withdrawal is achieved. Some treatment schedules for opioid dependence involved prolonged maintenance therapy with methadone where the daily dose is adjusted carefully for the individual.

The dose of Biodone Forte required is to be measured accurately, using a calibrated dropper or other appropriate method.

Dilution may be required by local protocols and this dilution should be made with distilled water if the solution is for immediate consumption, or with a solution containing 0.1% sodium benzoate for takeaway doses, which should be used within five days of preparation. Dilution of takeaway doses, usually to 200 mL, is a strategy intended to reduce the likelihood of injection and of small children consuming sufficient of the drug to cause overdose. takeaway solutions should be packaged in registered Quinex containers and sealed with a childproof cap.

OVERDOSAGE

Symptoms and signs

The symptoms and signs of overdose with methadone parallel these for other opioids, namely profound respiratory depression, pin-point pupils, hypotension circulatory failure and pulmonary oedema and coma.

Mydriasis may replace miosis as asphyxia intervenes. Drowsiness, floppiness, pinpoint pupils and apnoea have been reported in children.

Treatment

General supportive measures, including ECG monitoring, should be employed as required. The specific opioid antagonist naloxone can be used for the reversal of coma and the restoration of spontaneous respiration. Intravenous infusion is the preferred route of administration in the management of methadone overdose because of the short half-life of naloxone relative to the longer half-life of methadone. Continuous infusion reduces the possibility of prolonged respiratory depression and the risk of relapse, which can occur suddenly. It should be noted that QT prolongation will not be reversed by naloxone.

In opioid dependent patients the administration of the usual dose of an opioid antagonist will precipitate an acute withdrawal syndrome. The severity of this syndrome will depend on the degree of physical dependence and the dose of the antagonist administered. The use of an opioid antagonist should be avoided if possible. If it must be used to treat respiratory depression in the physically dependent person the antagonist should be administered with extreme care and by titration with smaller than usual doses of the antagonist.

Patients should be monitored closely for at least 48 hours after apparent recovery in case of relapse, since the duration of action of the antagonist may be substantially shorter than that of methadone.

The use of the respiratory or central stimulants is not recommended.

Acidification of the urine will enhance urinary excretion of methadone.

Methadone is not dialysable by either peritoneal dialysis or haemodialysis.

PRESENTATION

Oral liquid containing methadone hydrochloride 5 mg/mL.

Pack sizes: 200 mL and 1000 mL in glass bottles

Storage: Store below 25°C. Protect from light. Do not freeze.

Schedule: S8 in all States.

NAME AND ADDRESS OF THE SPONSOR

McGaw Biomed Pty Ltd
Level 12, 83 Mount Street
NSW 2060


Updated February 2005.
### Possible drug interactions with methadone

<table>
<thead>
<tr>
<th>Drug</th>
<th>Status of interaction</th>
<th>Effect</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abacavir</td>
<td>Clinically important</td>
<td>Reduced methadone levels</td>
<td>Increased methadone metabolism</td>
</tr>
<tr>
<td>Alcohol</td>
<td>Clinically important</td>
<td>Increased sedation, increased respiratory depression. Combination may also have increased hepatotoxic potential</td>
<td>Additive central nervous system depression</td>
</tr>
<tr>
<td>Barbiturates</td>
<td>Clinically important</td>
<td>Reduced methadone levels. Increased sedation. Additive central nervous system (CNS) depression.</td>
<td>Barbiturates stimulate hepatic enzymes involved in methadone maintenance</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Clinically important</td>
<td>Enhanced sedative effect</td>
<td>Additive CNS depression</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>Clinically important</td>
<td>Antagonist effect or enhanced sedative and respiratory depression</td>
<td>Buprenorphine is a partial agonist of opiate receptors</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Clinically important</td>
<td>Reduced methadone levels</td>
<td>Carbamazepine stimulates hepatic enzymes involved in methadone metabolism</td>
</tr>
<tr>
<td>Chlornaphazine</td>
<td>Clinically important</td>
<td>Enhanced sedative effect</td>
<td>Additive CNS depression</td>
</tr>
<tr>
<td>Chloral hydrate</td>
<td>Clinically important</td>
<td>Enhanced sedative effect</td>
<td>Additive CNS depression</td>
</tr>
<tr>
<td>Chlormethiazole</td>
<td>Clinically important</td>
<td>Enhanced sedative effect</td>
<td>Additive CNS depression</td>
</tr>
<tr>
<td>Cimetidine</td>
<td>Two cases have been shown in patients taking methadone as analgesia</td>
<td>Possible increase in methadone plasma levels</td>
<td>Cimetidine inhibits hepatic enzymes involved in methadone metabolism</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>Case in a patient taking methadone</td>
<td>Enhanced sedative effect and respiratory depression requiring naloxone</td>
<td>Probably by inhibiting hepatic enzymes involved in methadone metabolism</td>
</tr>
<tr>
<td>Citramide</td>
<td>Theoretically might increase the speed of onset of methadone absorption but not the extent</td>
<td>Theoretically might increase the speed of onset of methadone absorption but not the extent</td>
<td>Possibly by reversing the delayed gastric emptying associated with opioids</td>
</tr>
<tr>
<td>Cyclazine and other sedating antihistamines (cyclazine is not available in Australia)</td>
<td>Clinically important</td>
<td>Anecdotal reports of injection of cyclazine with opioids causing hallucinations. Reports of injections of high doses of diphenhydramine to achieve ‘buzz’</td>
<td>Additive psychoactive effects. Antimuscarinic effects at high doses</td>
</tr>
<tr>
<td>Delavirdine</td>
<td>Theoretically might raise plasma methadone levels</td>
<td>Theoretically might raise plasma methadone levels</td>
<td></td>
</tr>
<tr>
<td>Desipramine</td>
<td>Clinically important</td>
<td>Raised desipramine levels by up to a factor of two.</td>
<td>Unknown mechanism not seen with other tricyclic antidepressants.</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>Clinically important</td>
<td>Reduced plasma levels of methadone</td>
<td>Increased methadone metabolism.</td>
</tr>
<tr>
<td>Other tricyclic antidepressants</td>
<td>Theoretical</td>
<td>Enhanced sedative effect which is dose dependent</td>
<td>Additive CNS depression</td>
</tr>
<tr>
<td>Didanosine</td>
<td>Clinically important</td>
<td>Reduced plasma levels of stavudine. No effect on methadone</td>
<td>Increased didanosine metabolism</td>
</tr>
<tr>
<td>Drug</td>
<td>Status of interaction</td>
<td>Effect</td>
<td>Mechanism</td>
</tr>
<tr>
<td>--------------------------</td>
<td>---------------------------------------------------------------------------------------</td>
<td>-------------------------------------------------</td>
<td>---------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Disulfiram</td>
<td>Avoid in combination with methadone formulations containing alcohol (check with manufacturer)</td>
<td>Very unpleasant reaction to alcohol which can be dangerous</td>
<td>Disulfiram inhibits metabolism of alcohol allowing metabolites to build up</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>In theory should interact but combination has not been studied</td>
<td>Increase in methadone levels</td>
<td>Decreased methadone metabolism</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>In theory the same as ketoconazole</td>
<td>Raised methadone levels</td>
<td>Decreased methadone metabolism</td>
</tr>
<tr>
<td>Fluoxetine/Sertraline</td>
<td>Clinically important but not as significant as for fluvoxamine</td>
<td>Raised methadone levels</td>
<td>Decreased methadone metabolism</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>Clinically important</td>
<td>Raised plasma methadone levels</td>
<td>Decreased methadone metabolism</td>
</tr>
<tr>
<td>Other SSRIs</td>
<td>Theoretical</td>
<td>Raised plasma methadone levels</td>
<td>Decreased methadone metabolism</td>
</tr>
<tr>
<td>Grapefruit juice</td>
<td>Should interact in theory and there have been several anecdotal reports.</td>
<td>Raised methadone levels</td>
<td>Decreased methadone metabolism</td>
</tr>
<tr>
<td>Indinavir</td>
<td>Clinically important</td>
<td>Raised methadone levels</td>
<td>Decreased methadone metabolism</td>
</tr>
<tr>
<td>Ketoconazole</td>
<td>Clinically important</td>
<td>Raised methadone levels</td>
<td>Decreased methadone metabolism</td>
</tr>
<tr>
<td>MAOI (including selegiline and moclobemide)</td>
<td>Severe with pethedine though unlikely with methadone and has never been described</td>
<td>CNS excitation, delirium, hyperpyrexia, convulsions, hypotension or respiratory depression</td>
<td>Unclear, avoid the combination if possible</td>
</tr>
<tr>
<td>Naltrexone</td>
<td>Clinically important</td>
<td>Blocks effect of methadone (long acting)</td>
<td>Opioid antagonist — competes for opiate receptors</td>
</tr>
<tr>
<td>Naloxone</td>
<td>Clinically important</td>
<td>Blocks effects of methadone (short-acting) but may be needed if overdose suspected</td>
<td>Opioid antagonist — competes for opiate receptors</td>
</tr>
<tr>
<td>Nelfinavir</td>
<td></td>
<td>Decreased methadone levels</td>
<td>Increased methadone metabolism</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>Clinically important</td>
<td>Decreased methadone levels</td>
<td>Increased methadone metabolism</td>
</tr>
<tr>
<td>Nifedipine</td>
<td>Has only been demonstrated in vitro.</td>
<td>Increased nifedipine levels</td>
<td>Methadone increases metabolism of nifedipine</td>
</tr>
<tr>
<td>Omeprazole</td>
<td>To date only demonstrated in animals</td>
<td>Increased methadone levels</td>
<td>Possibly an effect on methadone absorption from the gut.</td>
</tr>
<tr>
<td>Pentazocine</td>
<td></td>
<td>Antagonist effect or enhanced sedative and respiratory depression</td>
<td>Pentazocine is a partial agonist of opiate receptors with weak antagonist effect</td>
</tr>
<tr>
<td>Drug</td>
<td>Status of interaction</td>
<td>Effect</td>
<td>Mechanism</td>
</tr>
<tr>
<td>----------------------</td>
<td>----------------------------------------</td>
<td>---------------------------------------------</td>
<td>---------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Phenobarbitone</td>
<td>See barbiturates above</td>
<td>As for barbiturates</td>
<td>As for barbiturates</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Clinically important</td>
<td>Reduced methadone levels</td>
<td>Stimulates hepatic enzymes involved in methadone metabolism</td>
</tr>
<tr>
<td>Propanolol</td>
<td>To date only demonstrated in animals.</td>
<td>Enhanced lethality of toxic doses of opioids</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Significance in humans is not known.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Exercise caution when co-administering</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phenobarbitone</td>
<td>Clinically important</td>
<td>Reduced methadone levels</td>
<td>Stimulates hepatic enzymes involved in methadone metabolism</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Clinically important</td>
<td>Reduced methadone levels</td>
<td>Stimulates hepatic enzymes involved in methadone metabolism</td>
</tr>
<tr>
<td>Propanolol</td>
<td>Clinically important</td>
<td>Reduced plasma levels of stavudine.</td>
<td>Increased stavudine metabolism</td>
</tr>
<tr>
<td></td>
<td>No effect on methadone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rifampicin</td>
<td>Very important. Most patients are likely to be affected</td>
<td>Reduced methadone levels</td>
<td>Stimulates hepatic enzymes involved in methadone metabolism</td>
</tr>
<tr>
<td>Rifabutin</td>
<td>Occasionally clinically important</td>
<td>Decreased methadone levels</td>
<td>Increased methadone metabolism</td>
</tr>
<tr>
<td>Ritonavir</td>
<td>Clinically important</td>
<td>Ritonavir may decrease plasma methadone levels</td>
<td>Increased methadone metabolism</td>
</tr>
<tr>
<td>Stavudine</td>
<td>Clinically important</td>
<td>Reduced plasma levels of stavudine.</td>
<td>Increased stavudine metabolism</td>
</tr>
<tr>
<td></td>
<td>No effect on methadone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thioridazine</td>
<td>Clinically important</td>
<td>Enhanced sedative effect which is dose-dependent</td>
<td>Enhanced CNS depression</td>
</tr>
<tr>
<td>Other protease inhibitors</td>
<td>Theoretical</td>
<td>May raise or lower methadone plasma levels</td>
<td>Inhibits methadone metabolism</td>
</tr>
<tr>
<td>Urine acidifiers (eg, ascorbic acid — vitamin C)</td>
<td>Clinically important</td>
<td>Reduced plasma methadone levels</td>
<td>Increased urinary excretion of methadone</td>
</tr>
<tr>
<td>Urine alkalisers (eg, sodium bicarbonate)</td>
<td>Clinically important</td>
<td>Increased plasma methadone levels</td>
<td>Reduced urinary excretion of methadone</td>
</tr>
<tr>
<td>Zidovudine</td>
<td>Clinically important</td>
<td>Raised plasma levels of zidovudine.</td>
<td>Unknown</td>
</tr>
<tr>
<td>Zopiclone</td>
<td>Clinically important</td>
<td>Enhanced sedative and respiratory depressant effect</td>
<td>Additive CNS depression</td>
</tr>
<tr>
<td>Other opioid agonists</td>
<td>Clinically important</td>
<td>Enhanced sedative effect</td>
<td>Additive CNS depression</td>
</tr>
<tr>
<td>Other CNS depressant drugs (eg, neuroleptics, hyoscine)</td>
<td>Clinically important</td>
<td>Enhanced sedative effect which is dose dependent</td>
<td>Additive CNS depression</td>
</tr>
</tbody>
</table>

This table is based on the table published in Clinical guidelines and procedures for the use of methadone in the maintenance treatment of opioid dependence (National Drug Strategy, Australian Government Department of Health and Ageing, 2003), which in turn was based on a table in Drug misuse and dependence — guidelines on clinical management (Department of Health, The Scottish Office Department of Health, Welsh Office, Department of Health and Social Services Northern Ireland, 1999. Additional information has been added from Methadone interactions with HIV antiviral drugs: all the meds together in one big chart. Harm Reduction Coalition, New York. <http://harmreduction.org/issues/health/haartmeth/allmeds.html>
E Buprenorphine product information

This product information was supplied by the manufacturer, Reckitt Benckiser, in July 2005, and may have been updated since that time. For the most recent product information, check with Reckitt Benckiser, 44 Wharf Road, West Ryde, NSW 2114.

NAME OF THE DRUG
Subutex (buprenorphine)

0.4 mg, 2 mg and 8 mg sublingual tablets

Description
Subutex sublingual tablets contain buprenorphine hydrochloride.

Subutex is an uncoated tablet intended for sublingual administration. It is available in three dosage strengths, 0.4 mg, 2 mg and 8 mg buprenorphine. Each tablet also contains lactose, mannitol, starch-maize, povidone, citric acid anhydrous, sodium citrate, and magnesium stearate.

Buprenorphine hydrochloride is a white powder, weakly acidic with limited solubility in water (19.5 mg/mL at 37°C, pH 4.1). Chemically, buprenorphine is 21-Cyclopropyl-7α-[S]-1-hydroxy-1, 2, 2-trimethyl(propyl)-6,14-endo-ethano-6, 7, 8, 14-tetrahydrooripavine hydrochloride. Buprenorphine hydrochloride has the molecular formula C_{29}H_{41}NO_4HCl and the molecular weight is 504.09. The CAS number is 53152-21-9. The chemical structure of buprenorphine is:

![Chemical structure of buprenorphine](image)

PHARMACOLOGY

Pharmacodynamic properties

Buprenorphine is a μ (mu) opioid receptor partial agonist, κ (kappa) opioid receptor antagonist. Its activity in opioid maintenance treatment is attributed to its slow dissociation from the μ receptors in the brain which reduces craving for opioids and opiate withdrawal symptoms. This minimises the need of the addicted patient for illicit opiate drugs.

During clinical pharmacology studies in opiate-dependent subjects, buprenorphine demonstrated a ceiling effect on a number of parameters, including positive mood, “good effect”, and respiratory depression.

Pharmacokinetic properties

Absorption

When taken orally, buprenorphine undergoes first-pass metabolism with N-dealkylation and glucuroconjugation in the small intestine and the liver. The use of Subutex by the oral route is therefore inappropriate. Subutex tablets are for sublingual administration.

Plasma levels of buprenorphine increased with the sublingual dose of Subutex although the increases were not directly dose-proportional (Table 1). There was a wide inter-patient variability in the sublingual absorption of buprenorphine from Subutex tablets, but within subjects the variability was low.

| Table 1. Mean C_{max} and AUC of buprenorphine following single sublingual doses of Subutex tablets in 23 (16M, 7F) subjects |
|---|---|---|---|---|
| | 4 mg | 8 mg | 16 mg | 24 mg |
| | Subutex | Subutex | Subutex | Subutex |
| C_{max} (ng/mL) | (0.31–3.76) | (1.09–4.82) | (1.79–8.58) | (1.67–17.3) |
| AUC_{0–tn} h·ng/mL | (9.25–101.6) | (6.19–64.81) | (15.7–135) |

Compared with intravenous administration, the bioavailability of 0.4 mg and 0.8 mg sublingual buprenorphine tablet doses was 30%–35%. With 8 mg sublingual buprenorphine delivered as a solution the buprenorphine bioavailability compared to intravenous administration was 42%.

Distribution

The absorption of buprenorphine is followed by a rapid distribution phase (distribution half-life of 2 to 5 hours).

Buprenorphine is highly lipophilic which leads to rapid penetration of the blood-brain barrier. The drug is around 96% protein bound primarily to alpha and beta globulin.

Metabolism and elimination

In animals and man buprenorphine is metabolised by Phase 1 (oxidative) and Phase 2 (conjugation) reactions. It is oxidatively metabolized by N-dealkylation to norbuprenorphine by CYP 3A4. The reported K_{m} for buprenorphine for CYP 3A4 in human liver microsomes was 89 mM, and addition of specific inhibitors of CYP 3A4 (eg, ketoconazole, gestodene, nifedipine, norfluoxetine, ritonavir) inhibited formation of norbuprenorphine. There was no indication of the involvement of CYP 1A1, 1A2, 2A6, 2B6, 2C8, 2C9, 2C19, 2D6 and 2E1 in the N-dealkylation of buprenorphine. Buprenorphine was a weak competitive inhibitor of CYP 2D6 and CYP
3A4 (reported mean $K_i$ in human liver microsomes was 10.3 µM and 40.2 µM respectively). Norbuprenorphine is a µ (mu) agonist with weak intrinsic activity and is considered to be an inactive metabolite.

Elimination of buprenorphine is bi- or tri-exponential, with a long terminal elimination phase (mean half-life of 34.6 hours, range 20.4-72.9 hours), due in part to re-absorption of buprenorphine after intestinal hydrolysis of the conjugated metabolite, and in part to the highly lipophilic nature of the molecule.

Buprenorphine is essentially eliminated in the faeces by biliary excretion of the glucuron conjugated metabolites (70%), the rest being eliminated in the urine.

**Elderly:** No pharmacokinetic data in elderly patients are available

**CLINICAL TRIALS**

Efficacy and safety data for Subutex are primarily derived from two clinical trials of buprenorphine sublingual tablets (Studies CR96/005 and CR96/013). All trials used buprenorphine in conjunction with psychosocial counselling as part of a comprehensive addiction treatment program. There have been no clinical studies conducted to assess the efficacy of buprenorphine as the only component of treatment.

Study CR96/005: In a double-blind, double-dummy, flexible dose-ranging, parallel group, comparative, 13-week study, 405 opioid dependent subjects were randomized to receive daily Subutex sublingual tablets or methadone syrup. During Weeks 1–6, doses were individually titrated until a stable dose was achieved (to a maximum of 32 mg Subutex or 150 mg methadone). Induction over 7 days was too slow for Subutex and resulted in early drop-outs. Once an adequate clinical dose of Subutex was attained it was maintained. During Weeks 1-6, the most used daily dose of Subutex was 8 mg/day and the average prescribed dose of buprenorphine in Week 6 was 10.9 mg/day. During Weeks 7–13 Subutex was dosed on alternate days by doubling the daily dose, with placebo tablets administered on intervening days. The most used Subutex dose during this phase was 16 mg given every other day. Methadone was dosed daily throughout the study with the most used doses being 40 mg/day in Weeks 1–6 and 50 mg/day in Weeks 7-13. The average prescribed dose of methadone in Week 6 was 53 mg/day. Take-home doses were not permitted except on weekends. Daily or alternate day Subutex had similar efficacy to daily methadone. In both parts of the study there were no differences between the groups in the percentages of urine samples that were negative for opiates. The secondary efficacy parameters complemented the results of the primary parameters. Heroin use and heroin craving were reduced in both treatment groups and other measures reflecting problems associated with illicit drug use also improved with treatment and there were no treatment group differences overall and in the two phases of the study.

Study CR96/013: In a double-blind, multicentre, placebo-controlled study, 326 heroin-addicted subjects were randomly assigned to either placebo, Subutex 16 mg/day, or combination treatment of 16 mg buprenorphine + 4 mg naloxone (combination tablet) per day. For subjects randomized to active treatment, dosing began with one 8 mg tablet of Subutex on Day 1, followed by 16 mg (two 8 mg tablets) of Subutex on day 2. Subjects randomised to Subutex continued on 16 mg/day for four weeks. Subjects randomised to buprenorphine + naloxone were switched to the combination tablet on Day 3. Subjects were seen daily in the clinic (Monday through Friday) for dosing and efficacy assessments. Take home doses were permitted for the weekend or holidays only. Subjects received one hour of individual counselling per week and a single session of HIV education. The percentage of thrice-weekly urine samples that were negative for opiates was significantly higher for subjects treated with Subutex or the combination tablet than for those who received placebo.

**INDICATIONS**

Treatment of opiate dependence, including maintenance and detoxification, within a framework of medical, social and psychological treatment.

**CONTRAINDICATIONS**

- Hypersensitivity to buprenorphine or any other component of the tablet
- Children less than 16 years of age
- Severe respiratory or hepatic insufficiency
- Acute intoxication with alcohol or other CNS depressant
- Pregnant women
- Breastfeeding.

**PRECAUTIONS**

**General:** Subutex should be administered with caution in elderly or debilitated patients and those with severe impairment of hepatic, pulmonary, or renal function; myxoedema or hypothyroidism, adrenal cortical insufficiency (eg Addison's disease); CNS depression or coma; toxic psychoses; prostatic hypertrophy or urethral stricture; acute alcoholism; delirium tremens; or kyphoscoliosis.

Buprenorphine increases intrahepatic pressure as do other opiates. Therefore, caution should be exercised when Subutex is to be administered to patients with dysfunction of the biliary tract.

As with other opioids, caution is advised in patients using buprenorphine and having:
- Hypotension
- Prostatic hypertrophy and urethral stenosis.

As with other mu-opiate receptor agonists, the administration of Subutex may obscure the diagnosis or clinical course of patients with acute abdominal conditions.

**Respiratory depression:** Subutex is intended for sublingual use only. Significant respiratory depression has been associated with buprenorphine, particularly by the intravenous
route. A number of deaths have occurred when addicts have intravenously misused buprenorphine, usually with benzodi- azepines concomitantly. Deaths have also been reported in association with concomitant administration of buprenor- phine with other depressants such as alcohol or other opio- ids. Patients should be warned of the potential danger of the self-administration of benzodiazepines or other CNS depres- sants at the same time as receiving Subutex.

In the event of depression of respiratory or cardiac function, primary attention should be given to the re-establishment of adequate respiratory exchange through provision of a patent airway and institution of assisted or controlled ventilation. Oxygen, intravenous fluids, vaspressors, and other supportive measures should be employed as indicated. High doses of naloxone hydrochloride 10–35 mg/70 kg may be of limited value in the management of buprenorphine overdose.

Subutex should be used with caution in patients with compro- mised respiratory function (eg, chronic obstructive pulmonary disease, cor pulmonale, decreased respiratory reserve, hypoxia, hypercapnia, or pre-existing respiratory depression).

Patients receiving Subutex in the presence of other narcotic analgesics, general anesthetics, benzodiazepines, phenothi- azines, other tranquilizers, sedative/hypnotics or other CNS depressants (including alcohol) may exhibit increased CNS depression. When such combined therapy is contemplated, reduction of the dose of one or both agents should be con- sidered. Subutex should be used cautiously with MAOIs, based on experience with morphine.

Hepatitis, hepatic events: Hepatic necrosis and hepatitis with jaundice have been reported. The spectrum of abnormalities ranges from transient asymptomatic elevations in hepatic transaminases to cases reports of hepatic failure, hepatic necro- sis, hepatorenal syndrome, and hepatic encephalopathy. Seri- ous cases of acute hepatic injury have also been reported in a context of misuse, especially by the intravenous route. These hepatic injuries were dose-related, and could be due to mito- chondrial toxicity. Pre-existing or acquired mitochondrial impairment (genetic diseases, viral infections particularly chronic hepatitis C, alcohol abuse, anorexia, associated mito- chondrial toxins, eg, aspirin, isoniazid, valproate, amiodarone, antiviral nucleoside analogues) could promote the occurrence of such hepatic injuries. These co-factors must be taken into account before prescribing Subutex and during treatment monitoring. Measurements of liver function tests prior to initi- ation of treatment is recommended to establish a baseline. Periodic monitoring of liver function tests during treatment is also recommended. A biological and etiological evaluation is recommended when a hepatic event is suspected. Depending upon the findings, the medicinal product may be discontinued cautiously so as to prevent withdrawal syndrome and to pre- vent a return to drug addiction. If the drug treatment is con- tinued, hepatic function should be monitored closely.

Hepatic disease: Because buprenorphine is metabolised by the liver, its activity may be increased and/or extended in those individuals with impaired hepatic function. Naloxone metabolism may also be impaired in hepatic failure patients. Because hepatic elimination plays a relatively large role (~70%) in the overall clearance of Subutex, lower initial doses and cautious titration of dosage may be required in patients with hepatic dysfunction.

**CYP3A4 inhibitors:** Because CYP3A4 inhibitors may increase concentrations of buprenorphine, patients already treated with CYP3A4 inhibitors should have their dose of Subutex titrated carefully since a reduced dose may be required in these patients (see Interactions with other drugs).

Renal disease: Renal elimination plays a relatively small role (~30%) in the overall clearance of Subutex. Therefore no dose modification based on renal function is required. Metabolites of buprenorphine accumulate in patients with renal failure. Caution is recommended when dosing patients with severe renal impairment (CLcr <30 mL/min).

Use in ambulatory patients: Subutex may impair the mental or physical abilities required for the performance of potentially dangerous tasks such as driving a car or operating machinery. Patients should be cautioned accordingly. Like other opiates, Subutex may produce orthostatic hypotension in ambulatory patients.

Head injury and increased intracranial pressure: Subu- tex, like other potent opiates may itself elevate cerebrospinal fluid pressure and should be used with caution in patients with head injury, intracranial lesions and other circumstances where cerebrospinal pressure may be increased. Subutex can produce miosis and changes in the level of consciousness that may interfere with patient evaluation.

Opiate withdrawal effects: Subutex may produce with- drawal symptoms in opiate dependent subjects if it is admin- istered too soon after another opiate. Discontinuation of treatment may result in a withdrawal syndrome that may be delayed.

Studies in animals, as well as clinical experience, have showed that buprenorphine may produce dependence but at a lower level than morphine. Consequently, it is important to follow the DOSAGE AND ADMINISTRATION recom- mendations.

Neonatal abstinence syndrome: Neonatal withdrawal has been reported in the infants of women treated with Subutex during pregnancy. Time to onset of withdrawal symptoms ranged from Day 1 to Day 8 of life with most (69%) occur- ring on Day 1. Adverse events associated with neonatal with- drawal syndrome included hypertonia, neonatal tremor, neonatal agitation, and myoclonus. There have been rare reports of convulsions and in one case, apnoea and brady- cardia were also reported. In many cases the withdrawal was serious and required treatment (See Use in pregnancy).

Allergic reactions: Cases of acute and chronic hypersensi- tivity to buprenorphine have been reported both in clinical trials and in the post-marketing experience. The most common signs and symptoms include rashes, hives, and pruritus. Cases of bronchospasm, angioneurotic oedema, and anaphylactic shock have been reported. A history of hypersensitiv- ity to buprenorphine is a contraindication to Subutex.
Carcinogenicity and mutagenicity

Carcinogenicity: Studies conducted in animals (rats and mice) show that buprenorphine is not carcinogenic at oral doses of up to 56 and 100 mg/kg/day, respectively, both of which equate to approximately 16 fold human exposure at the maximum recommended clinical dose of 32 mg based on body surface area.

Mutagenicity: The conclusion from Ames tests, chromosome aberration studies and a mouse lymphoma assay is that buprenorphine is not mutagenic in any of these test systems.

Impairment of fertility

There were no effects on mating performance or on fertility of male rats following short term treatment with buprenorphine at systemic exposures up to 38 times the maximum anticipated human exposure (based on plasma AUC).

Use in pregnancy (Category C)

Treatment with buprenorphine during pregnancy was associated with difficult parturition and fetotoxicity, including post-implantation loss and decreased postnatal survival, in rats and rabbits at systemic exposures similar to the maximum anticipated human exposure (32 mg/day). Evidence for teratology was not evident in animal studies.

Maternal oral administration at high doses (80 mg/kg/day) during gestation and lactation resulted in a delayed postnatal development of some neurological functions (surface righting reflex and startle response) in neonatal rats with a NOEL of 8 mg/kg/day PO (representing a systemic exposure of ~30% of the maximum anticipated clinical exposure).

Continued use of heroin during pregnancy is associated with significant risk to the mother and the fetus and neonate.

There are no adequate and well controlled studies of Subutex in pregnant women. Buprenorphine readily crosses the placental barrier, and may cause respiratory depression in neonates. During the last three months of pregnancy, chronic use of buprenorphine may be responsible for a withdrawal syndrome in neonates. Subutex is contraindicated in pregnant women (see CONTRAINDICATIONS).

Use in lactation

Animal studies indicate buprenorphine has the potential to inhibit lactation or milk production. Decreases in postnatal survival, growth and development were also observed in animals treated with buprenorphine during lactation. Because buprenorphine passes into the mother’s milk, Subutex should not be used in breastfeeding women.

Use in children

Subutex is not recommended for use in children. The safety and effectiveness of Subutex in subjects below the age of 16 has not been established.

Interactions with other drugs

A number of deaths and cases of coma have occurred when addicts have intravenously misused buprenorphine and benzodiazepines concomitantly. Patients should be warned of the potential danger of the intravenous self-administration of benzodiazepines or other CNS depressants at the same time as receiving Subutex (see PRECAUTIONS).

CYP3A4 inhibitors: An interaction study of buprenorphine with ketoconazole (a potent inhibitor of CYP3A4) resulted in increased Cmax and AUC of buprenorphine (approximately 50% and 70% respectively) and, to a lesser extent, of norbuprenorphine. Patients receiving Subutex should be closely monitored, and may require dose-reduction if combined with potent CYP3A4 inhibitors eg, protease inhibitors like ritonavir, neflavinavir or indinavir, azole antifungals like ketoconazole or itraconazole, calcium channel antagonists, and macrolide antibiotics (see PRECAUTIONS).

CYP3A4 inducers: The interaction of buprenorphine with CYP3A4 inducers has not been investigated, therefore it is recommended that patients receiving Subutex should be closely monitored if inducers (eg, phenobarbital, carbamazepine, phenytoin, rifampicin) are co-administered.

Effects on laboratory tests

Athletes should be aware that this medicine may cause a positive reaction to “anti-doping” tests.

ADVERSE REACTIONS

Adverse events reported to occur by at least 1% of patients being treated in clinical trials of Subutex (CR96/005 and CR96/013) are shown in Table 2.

The most common adverse events reported were those related to withdrawal symptoms (eg, abdominal pain, diarrhea, muscle aches, anxiety, sweating). In patients with marked drug dependence, initial administration of buprenorphine can produce a withdrawal effect similar to that associated with naloxone.

As with other opiates, orthostatic hypotension can occur (see PRECAUTIONS).

Post-marketing experience with Subutex for treatment of opiate dependency has been associated with the following rare side effects: respiratory depression and coma, hallucinations, neonatal withdrawal syndrome, neonatal tremor, neonatal feeding disorder, fetal disorders, convulsions, confusion, miosis, weight decrease, asphyxia, hypoventilation, pruritus, angioedema, heart rate and rhythm disorders, and deaths.

Cases of hepatitis with jaundice, hepatic failure, hepatic necrosis, hepatorenal syndrome, hepatic encephalopathy, and asymptomatic elevations in hepatic transaminases have been reported (see PRECAUTIONS).

In cases of intravenous misuse, local reactions, sometimes septic, and potentially serious acute hepatitis have been reported.

Cases of acute or chronic hypersensitivity to buprenorphine have been reported with symptoms including rashes, hives, pruritus and reported cases of bronchospasm, angioneurotic
oedema, and anaphylactic shock. (see PRECAUTIONS and CONTRAINDICATIONS).

### DOSAGE AND ADMINISTRATION

Treatment with Subutex sublingual tablets is intended for adults and children aged 16 years or over who have agreed to be treated for addiction. When initiating Subutex treatment, the physician should be aware that it can precipitate withdrawal in opioid dependent patients if given too soon after the administration of heroin, methadone or another opiate. The route of administration of Subutex is sublingual. Physicians must advise patients that the sublingual route is the only effective and safe route of administration for this drug.

#### Method of administration

Subutex tablets should be placed under the tongue until dissolved. This usually occurs within 2 to 10 min. The initial dose of Subutex may precipitate a mild abstinence syndrome in opioid dependent subjects. This may last up to 24 hours, but resolves with continued daily administration of Subutex.

#### Starting Subutex

An adequate maintenance dose, titrated to clinical effectiveness, should be achieved as rapidly as possible to prevent undue opiate withdrawal symptoms due to inadequate dosage.

Prior to induction, consideration should be given to the type of opiate dependence (ie, long- or short-acting opiate), the time since last opiate use and the degree or level of opiate dependence.

**Patients taking street heroin (or other short-acting opiates):** When treatment starts the dose of Subutex should be taken at least 6 hours after the patient last used opiates or when the early signs of withdrawal appear. The recommended starting dose is 4 mg Subutex on day one, with a possible additional 4 mg depending on the individual patient’s requirement.

**Patients on methadone:** Before starting treatment with Subutex, the maintenance dose of methadone should be reduced to 30 mg per day. The first dose of Subutex should be taken at least 24 hours after the patient last used methadone. The initial 4 mg Subutex induction dose should ideally be administered when the early withdrawal signs are evident.

### Dosage adjustment and maintenance

The dose of Subutex should be increased progressively according to the clinical effect in the individual patient and should not exceed a maximum daily dose of 32 mg. The dosage is adjusted according to reassessments of the clinical and psychological status of the patient.

### Less than daily dosing of Subutex

After a satisfactory period of stabilisation has been achieved the frequency of dosing may be decreased to dosing every other day at twice the individually titrated daily dose. For

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**Table 2. Very common adverse events reported by at least 10% of subjects**

<table>
<thead>
<tr>
<th>System</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body as a whole</td>
<td>Headache, pain, withdrawal syndrome</td>
</tr>
<tr>
<td>Digestive system</td>
<td>Nausea</td>
</tr>
<tr>
<td>Nervous system</td>
<td>Insomnia</td>
</tr>
<tr>
<td>Skin and appendages</td>
<td>Sweating</td>
</tr>
</tbody>
</table>

**Common adverse events reported by at least 1% of subjects**

<table>
<thead>
<tr>
<th>System</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body as a whole</td>
<td>Asthenia, chills, fever, flu syndrome, hostility, infection, malaise, abdominal pain, back pain, chest pain, neck pain</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Migraine, palpitations, syncope, vasodilation</td>
</tr>
<tr>
<td>Digestive System</td>
<td>Anorexia, constipation, diarrhoea, dry mouth, dyspepsia, flatulence, gastrointestinal disorder, nausea/vomiting, tooth disorder, vomiting</td>
</tr>
<tr>
<td>Haemic and lymphatic system</td>
<td>Lymphadenopathy</td>
</tr>
<tr>
<td>Metabolic/nutritional disorder</td>
<td>Peripheral oedema</td>
</tr>
<tr>
<td>Musculo-skeletal system</td>
<td>Arthralgia, leg cramps, myalgia, bone pain, spasm (general)</td>
</tr>
<tr>
<td>Nervous system</td>
<td>Agitation, anxiety, depression, dizziness, hypertonia, nervousness, paranoid reaction, paresthesia, somnolence, thinking abnormal, tremor</td>
</tr>
<tr>
<td>Respiratory system</td>
<td>Bronchitis, cough increased, dyspnoea, pharyngitis, rhinitis, yawning</td>
</tr>
<tr>
<td>Skin and appendages</td>
<td>Rash</td>
</tr>
<tr>
<td>Special senses</td>
<td>Lacrimation disorder, mydriasis</td>
</tr>
<tr>
<td>Urogenital system</td>
<td>Dysmenorrhoea</td>
</tr>
</tbody>
</table>
example, a patient stabilised to receive a daily dose of 8 mg may be given 16 mg on alternate days, with no medication on the intervening days. However, the dose given on any one day should not exceed 32 mg.

In some patients, after a satisfactory period of stabilisation has been achieved, the frequency of dosing may be decreased to 3 times a week (for example on Monday, Wednesday and Friday). The dose on Monday and Wednesday should be twice the individually titrated daily dose, and the dose on Friday should be three times the individually titrated daily dose, with no medication on the intervening days. However, the dose given on any one day should not exceed 32 mg.

Reducing dosage and stopping treatment

The decision to discontinue therapy with Subutex should be made as part of a comprehensive treatment plan. A gradual dose taper over a period of 21 days is shown in Table 3.

Detoxification

Examples of two 10-day detoxification schedules using Subutex are shown in Tables 4 and 5. These have been used to treat subjects who wish to stop using heroin and do not want to undergo a prolonged period of maintenance treatment on Subutex.

In the first detoxification schedule heroin dependent subjects are transferred to Subutex at doses up to 8 mg/day. The dose of buprenorphine was gradually decreased in a flexible 10-day schedule (Table 4).

Table 3. Gradual dose taper schedule

<table>
<thead>
<tr>
<th>Week</th>
<th>Maintenance dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 mg</td>
<td>16 mg</td>
</tr>
<tr>
<td>1 16 mg</td>
<td>12 mg</td>
</tr>
<tr>
<td>2 8 mg</td>
<td>8 mg</td>
</tr>
<tr>
<td>3 4 mg</td>
<td>4 mg</td>
</tr>
</tbody>
</table>

A similar schedule employed Subutex treatment only on the first 5 days (Table 5). The Subutex dose was increased over the first 3 days and then decreased.

Table 5. Detoxification schedule 2

<table>
<thead>
<tr>
<th>DAY</th>
<th>Subutex (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>10 +/- 2</td>
</tr>
<tr>
<td>3</td>
<td>10 +/- 2</td>
</tr>
<tr>
<td>4</td>
<td>8 +/- 2</td>
</tr>
<tr>
<td>5</td>
<td>4</td>
</tr>
</tbody>
</table>

OVERDOSE

Manifestations of acute overdose include pinpoint pupils, sedation, hypotension, respiratory depression and death.

In the event of accidental overdose, general supportive measures should be instituted including close monitoring of respiratory and cardiac status of the patient. The major symptom requiring intervention is respiratory depression, which could lead to respiratory arrest and death. If the patient vomits, care must be taken to prevent aspiration of the vomitus.

Treatment

In the event of depression of respiratory or cardiac function, primary attention should be given to the re-establishment of adequate respiratory exchange through provision of a patent airway and institution of assisted or controlled ventilation. Oxygen, intravenous fluids, vasopressors, and other supportive measures should be employed as indicated. High doses of naloxone hydrochloride 10–35 mg/70 kg may be of limited value in the management of buprenorphine overdose.

The long duration of action of Subutex should be taken into consideration when determining the length of treatment needed to reverse the effects of an overdose.

PRESENTATION

Subutex is supplied as white, oval, sublingual tablets containing 0.4 mg, 2 mg and 8 mg buprenorphine. The tablets are packed in PVC/PVdC/Aluminium blister strips of 7 tablets in a pack size of 7 tablets.

Store below 25°C. Protect from prolonged exposure to light. Protect from moisture.

NAME AND ADDRESS OF SPONSOR

Reckitt Benckiser
44 Wharf Road
West Ryde NSW 2114

DATE OF THERAPEUTIC GOODS ADMINISTRATION (TGA) APPROVAL: 14 JANUARY 2003

Date of last TGA Notification: 21 August 2003
NAME OF THE DRUG

Suboxone sublingual tablets contain buprenorphine hydrochloride and naloxone hydrochloride at a ratio of 4:1 buprenorphine:naloxone.

DESCRIPTION

Suboxone is an uncoated tablet intended for sublingual administration. It is available in two dosage strengths, 2 mg buprenorphine + 0.5 mg naloxone and 8 mg buprenorphine + 2 mg naloxone. Each tablet also contains lactose, mannitol, maize-starch, povidone, citric acid anhydrous, sodium citrate, magnesium stearate, acesulfame potassium and lemon and lime flavour.

Buprenorphine hydrochloride is a white powder, weakly acidic with limited solubility in water (19.5 mg/mL at 37°C, pH 4.1). Chemically, it is 21-Cyclopropyl-7α-[S]-1-hydroxy-1,2,2-trimethylpropyl]-6,14-endo-ethano-6,7,8,14-tetrahydrooripavine hydrochloride. Buprenorphine hydrochloride has the molecular formula C_{29}H_{41}NO_{4}HCl and the molecular weight is 504.09. The CAS number is 53152-21-9.

Naloxone hydrochloride dihydrate is a white to slightly off-white powder that exists as the dihydrate and is soluble in water, in dilute acids and in strong alkali. Chemically, it is (-)-17-Allyl-4,5α-epoxy-3,14-dihydroxymorphinan-6-one hydrochloride dihydrate. Naloxone hydrochloride has the molecular formula C_{19}H_{21}NO_{4}HCl.2H_{2}O and the molecular weight is 399.87. The CAS number of naloxone hydrochloride dihydrate is 51481-60-8. The chemical structures of buprenorphine hydrochloride and naloxone hydrochloride dihydrate are:

PHARMACOLOGY

Pharmacodynamic properties

Buprenorphine is a μ (mu) opioid receptor partial agonist, κ (kappa) opioid receptor antagonist. Its activity in opioid maintenance treatment is attributed to its slow dissociation from the μ receptors in the brain which reduces craving for opioids and opiate withdrawal symptoms. This minimises the need of the addicted patient for illicit opiate drugs.

During clinical pharmacology studies in opiate dependent subjects, buprenorphine demonstrated a ceiling effect on a number of parameters, including positive mood, “good effect”, and respiratory depression.

Naloxone is an antagonist at μ (mu) opioid receptors. Because of its almost complete first pass metabolism, naloxone administered orally or sublingually has no detectable pharmacological activity. However, when administered intravenously to opiate dependent people, the presence of naloxone in Suboxone produces marked opiate antagonist effects and opiate withdrawal, thereby deterring intravenous abuse.

Pharmacokinetic properties

Absorption

When taken orally, buprenorphine undergoes first-pass metabolism with N-dealkylation and glucuron conjugation in the small intestine and the liver. The use of Suboxone by the oral route is therefore inappropriate. Suboxone tablets are for sublingual administration.

Plasma levels of buprenorphine and naloxone increased with the sublingual dose of Suboxone although the increases were not directly dose-proportional (Table 1). The levels of naloxone were too low to determine the area under the curve values. There was a wide inter-patient variability in the sublingual absorption of buprenorphine and naloxone from Suboxone tablets, but within subjects the variability was low. Naloxone did not appear to affect the pharmacokinetics of buprenorphine and Subutex and Suboxone are expected to deliver sim-
ilar plasma concentrations of buprenorphine with sublingual dosing.

<table>
<thead>
<tr>
<th>Table 1. Mean Cmax and AUC of buprenorphine and naloxone following single sublingual doses of Suboxone tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>4 mg Suboxone</strong> (4 mg buprenorphine + 1 mg naloxone)</td>
</tr>
<tr>
<td><strong>8 mg Suboxone</strong> (8 mg buprenorphine + 2 mg naloxone)</td>
</tr>
<tr>
<td><strong>16 mg Suboxone</strong> (16 mg buprenorphine + 4 mg naloxone)</td>
</tr>
<tr>
<td><strong>24 mg Suboxone</strong> (24 mg buprenorphine + 6 mg naloxone)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Buprenorphine</th>
<th>22</th>
<th>22</th>
<th>21</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmax, ng/mL</td>
<td>2.16(0.68–4.33)</td>
<td>3.33(1.10–6.36)</td>
<td>5.87(2.48–10.0)</td>
<td>6.44(3.43–10.5)</td>
</tr>
<tr>
<td>AUC_{0–t}, ng/mL</td>
<td>12.88(5.18–23.24)</td>
<td>22.14(8.62–44.11)</td>
<td>37.67(18.71–74.13)</td>
<td>47.55(24.23–96.43)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Naloxone</th>
<th>20</th>
<th>21</th>
<th>20</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmax, ng/mL</td>
<td>0.12(0.06–0.25)</td>
<td>0.23(0.09–0.42)</td>
<td>0.39(0.07–1.15)</td>
<td>0.47(0.08–1.02)</td>
</tr>
</tbody>
</table>

Naloxone did not affect the pharmacokinetics of buprenorphine and both Suboxone and Subutex deliver similar plasma concentrations of buprenorphine. Compared with intravenous administration, the mean absolute bioavailability of buprenorphine from sublingual Suboxone 8mg tablets was 13.6% (range 5.1-24.9%) and that of naloxone was approximately 3%.

**Distribution**

The absorption of buprenorphine is followed by a rapid distribution phase (distribution half-life of 2 to 5 hours). Following intravenous administration, naloxone is rapidly distributed (distribution half-life of around 4 minutes).

Buprenorphine is highly lipophilic which leads to rapid penetration of the blood-brain barrier. The drug is around 96% protein bound primarily to alpha and beta globulin. Naloxone is approximately 45% protein bound, primarily to alpha and beta globulin.

**Metabolism and elimination**

In animals and man buprenorphine is metabolised by Phase 1 (oxidative) and Phase 2 (conjugation) reactions. It is oxidatively metabolised by N-dealkylation to norbuprenorphine by CYP 3A4. In in vitro metabolic studies, addition of specific inhibitors of CYP 3A4 (eg, ketoconazole, gestodene, nifedipine, norfluoxetine, ritonavir) inhibited formation of norbuprenorphine (see also **PRECAUTIONS and Interactions with other drugs**). There was no indication of the involvement of CYP 1A1, 1A2, 2A6, 2B6, 2C8, 2C9, 2C19, 2D6 and 2E1 in the N-dealkylation of buprenorphine. Buprenorphine was a weak competitive inhibitor of CYP 2D6 and CYP 3A4. Norbuprenorphine is a μ (mu) agonist with weak intrinsic activity and is considered to be an inactive metabolite.

Naloxone undergoes direct glucuroconjugation to naloxone-3-glucuronide as well as N-dealkylation and reduction of the 6-oxo group.

Elimination of buprenorphine is bi- or tri-exponential, with a long terminal elimination phase (mean half-life of 34.6 hours, range 20.4–72.9 hours), due in part to re-absorption of buprenorphine after intestinal hydrolysis of the conjugated metabolite, and in part to the highly lipophilic nature of the molecule. Naloxone has a short elimination half-life (mean 1.1 hours, range 0.63–1.94 hours).

Buprenorphine is essentially eliminated in the faeces by biliary excretion of the glucuroconjugated metabolites (70%), the rest being eliminated in the urine. Naloxone is excreted in the urine.

**Elderly:** No pharmacokinetic data in elderly patients are available.

**Clinical trials**

All trials used buprenorphine in conjunction with psychosocial counselling as part of a comprehensive addiction treatment program. There have been no clinical studies conducted to assess the efficacy of buprenorphine as the only component of treatment.

Clinical pharmacology studies demonstrate an aversive effect if Suboxone is misused by the injection route by opioid
 dependent patients. However, there have been no clinical trials to demonstrate a reduction in injection episodes because of the inherent difficulties and ethics in obtaining realistic outcomes of such a measure in a controlled study environment. Efficacy and safety data for Suboxone are primarily derived from a one-year clinical trial, comprising a 4 week randomised double blind comparison of Suboxone, buprenorphine and placebo tablets followed by a 48 week safety study of Suboxone (Study CR96/013 + CR96/014).

In the double blind placebo and active controlled study, 326 heroin-addicted subjects were randomly assigned to either Suboxone 16 mg per day, 16 mg buprenorphine per day or placebo tablets. For subjects randomised to either active treatment, dosing began with one 8 mg tablet of buprenorphine on Day 1, followed by 16 mg (two 8 mg tablets) of buprenorphine on Day 2. On Day 3, those randomised to receive Suboxone were switched to the combination tablet. Subjects were seen daily in the clinic (Monday through Friday) for dosing and efficacy assessments. Take-home doses were provided for weekends. The primary study comparison was to assess the efficacy of buprenorphine and Suboxone individually against placebo. The percentage of thrice-weekly urine samples that were negative for non-study opioids was statistically higher for both Suboxone versus placebo ($P < 0.0001$) and buprenorphine versus placebo ($P < 0.0001$).

**INDICATIONS**

Treatment of opiate dependence within a framework of medical, social and psychological treatment.

**CONTRAINDICATIONS**

- hypersensitivity to buprenorphine or naloxone or any other component of the tablet
- children less than 16 years of age
- severe respiratory or hepatic insufficiency (Child-Pugh B or C)
- acute intoxication with alcohol or other CNS depressant.
- pregnant women
- breastfeeding.

**PRECAUTIONS**

**General:** Suboxone should be administered with caution in elderly or debilitated patients and those with impairment of hepatic, pulmonary, or renal function; myxoedema or hypothyroidism, adrenal cortical insufficiency (eg, Addison’s disease); CNS depression or coma; toxic psychoses; prostatic hypertrophy or urethral stricture; acute alcoholism; delirium tremens; or kyphoscoliosis.

Buprenorphine increases intrahepatic pressure as do other opiates. Therefore, caution should be exercised when Suboxone is to be administered to patients with dysfunction of the biliary tract.

As with other opioids, caution is advised in patients using buprenorphine and having:

- hypotension
- prostatic hypertrophy and urethral stenosis.

As with other mu-opiate receptor agonists, the administration of Suboxone may obscure the diagnosis or clinical course of patients with acute abdominal conditions.

**Respiratory depression:** Suboxone is intended for sublingual use only. Significant respiratory depression has been associated with buprenorphine, particularly by the intravenous route. A number of deaths have occurred when addicts have intravenously misused buprenorphine, usually with benzodiazepines concomitantly. Deaths have also been reported in association with concomitant administration of buprenorphine with other depressants such as alcohol or other opioids. Patients should be warned of the potential danger of the self-administration of benzodiazepines or other CNS depressants at the same time as receiving Suboxone.

In the event of depression of respiratory or cardiac function, primary attention should be given to the re-establishment of adequate respiratory exchange through provision of a patent airway and institution of assisted or controlled ventilation. Oxygen, intravenous fluids, vasopressors, and other supportive measures should be employed as indicated. High doses of naloxone hydrochloride 10–35 mg/70 kg may be of limited value in the management of buprenorphine overdose.

Suboxone should be used with caution in patients with compromised respiratory function (eg, chronic obstructive pulmonary disease, cor pulmonale, decreased respiratory reserve, hypoxia, hypercapnia, or pre-existing respiratory depression).

**CNS depression:** Patients receiving Suboxone in the presence of other narcotic analgesics, general anaesthetics, benzodiazepines, phenothiazines, other tranquillisers, sedative/hypnotics, or other CNS depressants (including alcohol) may exhibit increased CNS depression. When such combined therapy is contemplated, reduction of the dose of one or both agents should be considered. Suboxone should be used cautiously with MAOIs, based on experience with morphine.

**Hepatitis, hepatic events:** Hepatic necrosis and hepatitis with jaundice have been reported with buprenorphine use. The spectrum of abnormalities ranges from transient asymptomatic elevations in hepatic transaminases to case reports of hepatic failure, hepatic necrosis, hepatorenal syndrome, and hepatic encephalopathy. Serious cases of acute hepatic injury have also been reported in a context of misuse, especially by the intravenous route. These hepatic injuries were dose-related, and could be due to mitochondrial toxicity. Pre-existing or acquired mitochondrial impairment (genetic diseases, viral infections particularly chronic hepatitis C, alcohol abuse, anorexia, associated mitochondrial toxins — eg, aspirin, isoniazid, valproate, amiodarone, antiviral nucleoside analogues) could promote the occurrence of such hepatic injuries. These co-factors must be taken into account before prescribing Suboxone and during treatment monitoring. Measurements of
liver function tests prior to initiation of treatment is recommended to establish a baseline. Periodic monitoring of liver function tests during treatment is also recommended. A biological and etiological evaluation is recommended when a hepatic event is suspected. Depending upon the findings, the medicinal product may be discontinued cautiously so as to prevent withdrawal syndrome and to prevent a return to drug addiction. If the drug treatment is continued, hepatic function should be monitored closely.

**Hepatic disease:** Because buprenorphine is metabolised by the liver, its activity may be increased and/or extended in those individuals with impaired hepatic function. Naloxone metabolism may also be impaired in hepatic failure patients. Because hepatic elimination plays a relatively large role (~70%) in the overall clearance of Suboxone, lower initial doses and cautious titration of dosage may be required in patients with hepatic dysfunction.

**CYP3A4 inhibitors:** Because CYP3A4 inhibitors may increase concentrations of buprenorphine, patients already treated with CYP3A4 inhibitors should have their dose of Suboxone titrated carefully since a reduced dose may be required in these patients (see *Interactions with other drugs*).

**Renal disease:** Renal elimination plays a relatively small role (~30%) in the overall clearance of buprenorphine. Therefore no dose modification based on renal function is required. Metabolites of buprenorphine accumulate in patients with renal failure. Caution is recommended when dosing patients with severe renal impairment (CLcr < 30 mL/min).

**Use in ambulatory patients:** Suboxone may impair the mental or physical abilities required for the performance of potentially dangerous tasks such as driving a car or operating machinery. Patients should be cautioned accordingly. Like other opiates, Suboxone may produce orthostatic hypotension in ambulatory patients.

**Head injury and increased intracranial pressure:** Suboxone, like other potent opiates may itself elevate cerebrospinal fluid pressure and should be used with caution in patients with head injury, intracranial lesions and other circumstances where cerebrospinal pressure may be increased. Suboxone can produce miosis and changes in the level of consciousness that may interfere with patient evaluation.

**Opiate withdrawal effects:** Because Suboxone contains naloxone, it is highly likely to produce marked and intense opiate withdrawal symptoms if injected.

Suboxone may produce withdrawal symptoms in opiate dependent subjects if it is administered too soon after another opiate. Discontinuation of treatment may result in a withdrawal syndrome that may be delayed. Studies in animals, as well as clinical experience, have showed that buprenorphine may produce dependence but at a lower level than morphine. Consequently, it is important to follow the DOSAGE AND ADMINISTRATION recommendations.

**Neonatal abstinence syndrome:** Neonatal withdrawal has been reported in the infants of women treated with buprenorphine during pregnancy. Time to onset of withdrawal symptoms ranged from Day 1 to Day 8 of life with most (69%) occurring on Day 1. Adverse events associated with neonatal withdrawal syndrome included hypertonia, neonatal tremor, neonatal agitation, and myoclonus. There have been rare reports of convulsions and in one case, apnoea and bradycardia were also reported. In many cases the withdrawal was serious and required treatment (See *Use in pregnancy*).

**Allergic reactions:** Cases of acute and chronic hypersensitivity to buprenorphine have been reported both in clinical trials and in the post-marketing experience. The most common signs and symptoms include rashes, hives, and pruritus. Cases of bronchospasm, angioneurotic oedema, and anaphylactic shock have been reported. A history of hypersensitivity to buprenorphine or naloxone is a contraindication to Suboxone use.

**Carcinogenicity and mutagenicity**

**Carcinogenicity:** In mice, no evidence for carcinogenicity due to buprenorphine was noted in life-time studies at dietary doses of up to 100 mg/kg/day, which equates to ca 14-fold human exposure at the maximum recommended clinical dose of 32 mg based on body surface area.

In rats, statistically significant (trend test adjusted for survival) dose-related increases in testicular interstitial (Leydig) cell tumours occurred at a dietary buprenorphine dose of 55 mg/kg/day (16 fold the maximal recommended human sublingual dose of 32 mg, on a mg/m² basis); the no-effect dose was 5.4 mg/kg/day (twice the maximal human dose, on a mg/m² basis).

The carcinogenic potential of naloxone alone has not been investigated in long-term animal studies.

In a 2-year dietary study with Suboxone in rats, Leydig cell adenomas were found at doses of 6–115 mg/kg/day, associated with respective exposures (plasma AUC) to buprenorphine and naloxone of 2–21 fold, and up to 58 fold, anticipated human exposure. A NOEL was not established in the study.

**Mutagenicity:** In genotoxicity studies using buprenorphine and naloxone (9:2), assays for bacterial gene mutations and chromosomal damage (human lymphocytes in vitro and rat micronucleus test in vivo) were negative.

**Impairment of fertility**

There were no effects on mating performance or fertility in rats following buprenorphine treatment at oral doses ca 20 times the maximum clinical dose of 32 mg/kg/day (based on mg/m²). Dietary administration of Suboxone to rats at doses of 47 mg/kg/day or greater (estimated respective buprenorphine and naloxone exposures 14 and 24 times the anticipated clinical exposure, based on plasma AUC) resulted in reduced female conception rates. A dietary dose of 9.4 mg/kg/day (twice the anticipated clinical exposure for both buprenorphine (based on AUC) and naloxone (based on mg/m²) had no adverse effect on fertility.
Use in pregnancy (Category C)

In rats, oral administration of buprenorphine at doses up to 20 times the maximum clinical dose of 32 mg/day (based on mg/m²) prior to and during gestation and lactation resulted in reduced implantation, fewer live births, and reduced pup weight gain and survival. There was no evidence of teratogenicity in rats and rabbits following parenteral administration of buprenorphine during the period of organogenesis, although there was embryofoetal toxicity, and reduced pup viability and developmental delays in rats. There was no evidence of teratogenicity in rats and rabbits following oral or intramuscular administration of maternally toxic doses of combinations of buprenorphine + naloxone during the period of organogenesis, although post-implantation losses were increased. In rats, oral (20 times maximum clinical dose, based on mg/m²) or intramuscular administration of buprenorphine from late gestation to weaning was associated with increased stillbirths, reduced postnatal survival, and delayed postnatal development including weight gain and some neurological functions (surface righting reflex and startle response).

There are no adequate or well controlled studies of Suboxone in pregnant women. Buprenorphine readily crosses the placental barrier, and may cause respiratory depression in neonates. During the last three months of pregnancy, chronic use of buprenorphine may be responsible for a withdrawal syndrome in neonates. Suboxone is contraindicated in pregnancy (see CONTRAINDICATIONS). Continued use of heroin during pregnancy is associated with significant risk to the mother and the fetus and neonate.

Use in lactation

Animal studies indicate buprenorphine has the potential to inhibit lactation or milk production. In rats, oral (20 times maximum clinical dose, based on mg/m²) or intramuscular administration of buprenorphine from late gestation to weaning was associated with increased stillbirths, reduced postnatal survival, and delayed postnatal development including weight gain and some neurological functions (surface righting reflex and startle response). The no effect level for developmental effects was twice the maximum clinical dose, based on mg/m². Because buprenorphine is excreted into human milk, Suboxone should not be used in breastfeeding women.

Use in children

Suboxone is not recommended for use in children. The safety and effectiveness of Suboxone in subjects below the age of 16 has not been established.

Interactions with other drugs

A number of deaths and cases of coma have occurred when addicts have intravenously misused buprenorphine and benzodiazepines concomitantly. Patients should be warned of the potential danger of the intravenous self-administration of benzodiazepines or other CNS depressants at the same time as receiving Suboxone (see PRECAUTIONS).

<table>
<thead>
<tr>
<th>Common adverse events reported by at least 1% of subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body as a whole</td>
</tr>
<tr>
<td>Cardiovascular system</td>
</tr>
<tr>
<td>Digestive system</td>
</tr>
<tr>
<td>Metabolic/nutritional disorders</td>
</tr>
<tr>
<td>Musculoskeletal system</td>
</tr>
<tr>
<td>Nervous system</td>
</tr>
<tr>
<td>Respiratory system</td>
</tr>
<tr>
<td>Skin and appendages</td>
</tr>
<tr>
<td>Special senses</td>
</tr>
<tr>
<td>Urogenital system</td>
</tr>
</tbody>
</table>

CYP3A4 inhibitors: An interaction study of buprenorphine with ketoconazole (a potent inhibitor of CYP3A4) resulted in increased Cₘₐₓ and AUC of buprenorphine (approximately 50% and 70% respectively) and, to a lesser extent, of norbuprenorphine. Patients receiving Suboxone should be closely monitored, and may require dose-reduction if combined with potent CYP3A4 inhibitors eg, protease inhibitors like ritonavir, ne菲尔avir or indinavir, azole antifungals like ketoconazole or itraconazole, calcium channel antagonists, and macrolide antibiotics (see PRECAUTIONS).

CYP3A4 inducers: The interaction of buprenorphine with CYP3A4 inducers has not been investigated; therefore it is
recommended that patients receiving Suboxone should be closely monitored if inducers (eg, phenobarbital, carba-
mazepine, phenytoin, rifampicin) are co-administered.

Effects on laboratory tests
Athletes should be aware that this medicine may cause a positive reaction to “anti-doping” tests.

Adverse reactions
Adverse events reported to occur by at least 1% of patients being treated in clinical trials of Suboxone (CR96/013 + CR96/014) are shown in Table 2.

The most common adverse events reported were those related to withdrawal symptoms (eg, abdominal pain, diarrhoea, muscle aches, anxiety, sweating). In patients with marked drug dependence, initial administration of buprenor-
phine can produce a withdrawal effect similar to that associated with naloxone.

As with other opiates, orthostatic hypotension can occur (see PRECAUTIONS).

Post-marketing experience with buprenorphine alone and Suboxone
Post-marketing experience with buprenorphine alone for treatment of opiate dependency has been associated with the following rare side effects: respiratory depression and coma, hallucinations, neonatal withdrawal syndrome, neo-
natal tremor, neonatal feeding disorder, fetal disorders, convulsions, confusion, miosis, weight decrease, asphyxia, hypoventilation, pruritus, angioedema, heart rate and rhythm disorders, and deaths.

Additionally, post-marketing experience with Suboxone for treatment of opiate dependency has been associated rarely with the following side effects: insomnia, reduced feeling, anorexia (see also Table 2 above), amnesia, convulsions, blood in vomit, fatigue, jaundice, swollen joints, miscarriage, shortness of breath, and suicide ideation.

Cases of hepatitis with jaundice, hepatic failure, hepatic necrosis, hepatorenal syndrome, hepatic encephalopathy, and asymptomatic elevations in hepatic transaminases have been reported with buprenorphine use (see PRECAUTIONS).

In cases of intravenous misuse of buprenorphine, local reac-
tions, sometimes septic, and potentially serious acute hepatitis have been reported.

Cases of acute or chronic hypersensitivity have been reported with buprenorphine with symptoms including rashes, hives, pruritus and reported cases of bronchospasm, angioneurotic oedema, and anaphylactic shock. (see PRECAUTIONS and CONTRAINDICATIONS).

DOSAGE AND ADMINISTRATION
Treatment with Suboxone sublingual tablets is intended for adults and children aged 16 years or over who have agreed to be treated for addiction. When initiating Suboxone treatment, the physician should be aware that it can precipitate with-
drawal in opioid dependent patients if given too soon after the administration of heroin, methadone or another opiate.

The route of administration of Suboxone is sublingual. Sub-
oxone tablets should not be swallowed as this reduces the bioavailability of the medicine. Physicians must advise patients that the sublingual route is the only effective and safe route of administration for this drug.

Please note: The following instructions refer to the buprenorphine content of each dose. Suboxone 8 mg/2 mg (buprenorphine–naloxone) is referred to as the 8 mg dose and Suboxone 2 mg/0.5 mg (buprenorphine–naloxone) is referred to as the 2 mg dose.

Method of administration
Suboxone tablets are to be placed under the tongue until dissolved, which usually requires 2 to 10 minutes. The dose is made up from 2 mg and 8 mg sublingual tablets, which may be taken all at the same time or in two divided portions; the second portion to be taken directly after the first portion has dissolved.

Starting Suboxone
An adequate maintenance dose, titrated to clinical effective-
ness, should be achieved as rapidly as possible to prevent undue opiate withdrawal symptoms due to inadequate dos-

age.

Prior to induction, consideration should be given to the type of opiate dependence (ie, long- or short-acting opiate), the time since last opiate use and the degree or level of opiate dependence.

Induction onto Subutex (buprenorphine tablets) is recom-

mended when there is doubt about the level of dependence or previous drug use, to avoid precipitating opiate withdrawal. Patients can be switched to Suboxone on the third day.

Patients taking street heroin (or other short-acting opi-

ates): When treatment starts the dose of Suboxone should be taken at least 6 hours after the patient last used opiates or when the early signs of withdrawal appear. The recom-

mended starting dose is 4 mg Suboxone on Day One, with a possible additional 4 mg depending on the individual patient’s requirement.

Patients on methadone: Before starting treatment with Suboxone, the maintenance dose of methadone should be reduced to a maximum of 30 mg per day. The first dose of Suboxone should be taken at least 24 hours after the patient last used methadone. The initial 4 mg Suboxone induction dose should ideally be administered when early signs of withdrawal are evident.

Dosage adjustment and maintenance
The dose of Suboxone should be increased progressively according to the clinical effect in the individual patient and
should not exceed a maximum daily dose of 32 mg. The dosage is adjusted according to reassessments of the clinical and psychological status of the patient.

**Less-than-daily dosing of Suboxone**

After a satisfactory period of stabilisation has been achieved the frequency of dosing may be decreased to dosing every other day at twice the individually titrated daily dose. For example, a patient stabilised to receive a daily dose of 8 mg may be given 16 mg on alternate days, with no medication on the intervening days. However, the dose given on any one day should not exceed 32 mg.

In some patients, after a satisfactory period of stabilisation has been achieved, the frequency of dosing may be decreased to 3 times a week (for example on Monday, Wednesday and Friday). The dose on Monday and Wednesday should be twice the individually titrated daily dose, and the dose on Friday should be three times the individually titrated daily dose, with no medication on the intervening days. However, the dose given on any one day should not exceed 32 mg.

**Reducing dosage and stopping treatment**

The decision to discontinue therapy with Suboxone should be made as part of a comprehensive treatment plan. A gradual dose taper over a period of 21 days is shown in Table 3.

<table>
<thead>
<tr>
<th>Week</th>
<th>20 mg maintenance dose</th>
<th>16 mg maintenance dose</th>
<th>8 mg maintenance dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16 mg</td>
<td>12 mg</td>
<td>8 mg</td>
</tr>
<tr>
<td>2</td>
<td>8 mg</td>
<td>8 mg</td>
<td>4 mg</td>
</tr>
<tr>
<td>3</td>
<td>4 mg</td>
<td>4 mg</td>
<td>4 mg</td>
</tr>
</tbody>
</table>

**Overdosage**

Manifestations of acute overdose include pinpoint pupils, sedation, hypotension, respiratory depression and death.

In the event of accidental overdose, general supportive measures should be instituted including close monitoring of respiratory and cardiac status of the patient. The major symptom requiring intervention is respiratory depression, which could lead to respiratory arrest and death. If the patient vomits, care must be taken to prevent aspiration of the vomitus.

**Treatment**

In the event of depression of respiratory or cardiac function, primary attention should be given to the re-establishment of adequate respiratory exchange through provision of a patent airway and institution of assisted or controlled ventilation. Oxygen, intravenous fluids, vasopressors, and other supportive measures should be employed as indicated. High doses of naloxone hydrochloride 10–35 mg/70 kg may be of limited value in the management of buprenorphine overdose.

The long duration of action of Suboxone should be taken into consideration when determining the length of treatment needed to reverse the effects of an overdose.

**PRESENTATION**

Suboxone is supplied as white, hexagonal sublingual tablets containing 2 mg buprenorphine + 0.5 mg naloxone and 8 mg buprenorphine + 2 mg naloxone. The tablets are packed in aluminium/aluminium blister strips of 7 tablets in a pack size of 28 tablets.

Store below 30°C.

**NAME AND ADDRESS OF SPONSOR**

Reckitt Benckiser
44 Wharf Road
West Ryde NSW 2114

Date of Therapeutic Goods Administration (TGA) approval: 27 July 2005
## Possible drug interactions with buprenorphine or buprenorphine–naloxone

<table>
<thead>
<tr>
<th>Drug</th>
<th>Status of interaction</th>
<th>Effect</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>Clinically important</td>
<td>Increased sedation, increased respiratory depression. Combination may also have increased hepatotoxic potential.</td>
<td>Additive central nervous system depression</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Clinically important</td>
<td>Enhanced sedative effect</td>
<td>Additive CNS depression</td>
</tr>
<tr>
<td>Methadone and other opioids</td>
<td>Clinically important</td>
<td>Buprenorphine's antagonist effect may precipitate withdrawal in patients taking other opioids, or enhanced sedative and respiratory depression</td>
<td>Buprenorphine is a partial agonist of opiate receptors.</td>
</tr>
<tr>
<td>Naltrexone and naloxone</td>
<td>Clinically important</td>
<td>Greatly reduced antagonist effect of naltrexone and naloxone</td>
<td>Buprenorphine has higher affinity for opioid receptors than naltrexone and naloxone</td>
</tr>
<tr>
<td><strong>Drugs that inhibit CYP 3A4</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erythromycin and other macrolide antibiotics</td>
<td>Clinically important</td>
<td>Raised buprenorphine levels</td>
<td>Decreased buprenorphine metabolism</td>
</tr>
<tr>
<td>HIV protease inhibitors such as indinavir, ritonavir, saquinavir</td>
<td>Clinically important</td>
<td>Raised buprenorphine levels</td>
<td>Decreased buprenorphine metabolism</td>
</tr>
<tr>
<td>Ketoconazole and other azole antifungal agents</td>
<td>Clinically important</td>
<td>Raised buprenorphine levels</td>
<td>Decreased buprenorphine metabolism</td>
</tr>
<tr>
<td><strong>Drugs that induce CYP 3A4</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Theoretical</td>
<td>Reduced buprenorphine levels</td>
<td>Increased buprenorphine metabolism</td>
</tr>
<tr>
<td>Barbiturates, eg phenobarbitone</td>
<td>Clinically important</td>
<td>Reduced buprenorphine levels. Increased sedation. Additive CNS depression</td>
<td>Increased buprenorphine metabolism</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Theoretical</td>
<td>Reduced buprenorphine levels</td>
<td>Increased buprenorphine metabolism</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>Theoretical</td>
<td>Reduced buprenorphine levels</td>
<td>Increased buprenorphine metabolism</td>
</tr>
</tbody>
</table>
Routine screening for domestic violence is a key element of the NSW Health policy and procedures for identifying and responding to domestic violence.

Further information
NSW Health Routine for Domestic Violence Program
NSW HEALTH
SCREENING FOR DOMESTIC VIOLENCE

Health Worker to complete this form.

Medical Record Number __________________________ Date __________/________/________

Explain:
• In this Health Service we ask all women the same questions about violence at home.
• This is because violence in the home is very common and can be serious and we want to improve our response to women experiencing domestic violence.
• You don’t have to answer the questions if you don’t want to.
• What you say will remain confidential to the Health Service except where you give us information that indicates there are serious safety concerns for you or your children.

Ask:
Q1. Within the last year have you been hit, slapped or hurt in other ways by your partner or ex-partner? [ ] YES [ ] NO
Q2. Are you frightened of your partner or ex-partner? [ ] YES [ ] NO

If the woman answers NO to both questions, give the information card to her and say:
Here is some information that we are giving to all women about domestic violence.

If the woman answers YES to either or both of the above questions continue to question 3 and 4.
Q3. Are you safe to go home when you leave here? [ ] YES [ ] NO
Q4. Would you like some assistance with this? [ ] YES [ ] NO

Consider safety concerns raised in answers to questions.

Complete:

<table>
<thead>
<tr>
<th>Action taken</th>
<th>Screening was not completed due to</th>
</tr>
</thead>
<tbody>
<tr>
<td>Domestic violence identified, information given</td>
<td>Presence of partner</td>
</tr>
<tr>
<td>Domestic violence identified, information declined</td>
<td>Presence of other family members</td>
</tr>
<tr>
<td>Domestic violence not identified, information given</td>
<td>Woman declined to answer the questions</td>
</tr>
<tr>
<td>Domestic violence not identified, information declined</td>
<td>Other reason (specify) _____________</td>
</tr>
<tr>
<td>Support given and options discussed</td>
<td>Signature of Staff __________________</td>
</tr>
<tr>
<td>Reported to DoCS</td>
<td>Name ____________________________</td>
</tr>
<tr>
<td>Police notified</td>
<td>Designation _______________________</td>
</tr>
<tr>
<td>Referral made to ____________________________</td>
<td>____________________________</td>
</tr>
<tr>
<td>Other action taken ____________________________</td>
<td>____________________________</td>
</tr>
<tr>
<td>Other violence/abuse disclosed ____________________________</td>
<td>____________________________</td>
</tr>
</tbody>
</table>
Routine screening for domestic violence

Data collection snapshot 2003
To: All services and facilities which have commenced screening for domestic violence

The NSW Health Policy and Procedures for Identifying and Responding to Domestic Violence (2003) requires the introduction of routine screening of eligible women for domestic violence in maternity, early childhood, mental health, and alcohol and other drugs services by the end of 2004.

The Domestic Violence Policy identifies the need for Area Health Services to participate in data collection processes, which document the level and outcomes of screening. To make this process as straightforward as possible, the data collection will take the form of an annual snapshot over a one-month period in each service facility that has commenced screening. The 2003 snapshot will occur 1-30 November 2003 inclusive.

Each facility, which has commenced screening, is asked to complete the attached proforma and submit to the Area Health Service for forwarding to the Department by 10 December 2003.

For further information or an electronic format (Excel), the officer to contact is Gwen Cosier, A/Senior Policy Analyst, on 9391 9905 or gcosi@doh.health.nsw.gov.au.

Explanatory notes for completing data snapshot form:

1. Whole numbers or percentages only are required.
2. ‘Service’ refers to the broad program area eg early childhood, alcohol and other drug service.
3. ‘Facility’ refers to the specific service, unit or site eg X Antenatal Clinic, Y Community Mental Health Centre.
4. Please note a contact person for the screening facility, with contact details.
5. Column 1 asks for total numbers of eligible women presenting during 1-30 November inclusive. This means all women attending antenatal and early childhood services, and women aged 16 and over attending mental health, alcohol and other drugs, or other services.
6. Column 2 asks for total numbers of all eligible women who were screened.
7. Column 3 is the percentage of eligible women attending the service who were screened.
8. Column 4 is the total number of women who answered, ‘yes’ to either or both of questions 1 and 2 on the screening form, thereby identifying positive for domestic violence.
9. Column 5 is the number of women who identified positive to domestic violence and accepted some form of assistance.
10. The ‘Action taken: referral’ section asks for total numbers of Police notifications, Department of Community Services reports, and other referrals. Count all such referrals. Individual women may be in more than one category.
11. The ‘Screening not completed due to:’ section asks for facilities to note the reasons why screening may not have been completed.
**Routine Screening for Domestic Violence: Snapshot 1 November - 30 November 2003**

<table>
<thead>
<tr>
<th>Area:</th>
<th>Service:</th>
<th>Facility:</th>
<th>Date screening commenced:</th>
<th>Service contact person:</th>
<th>Phone:</th>
<th>Email:</th>
<th>Action taken: referral</th>
<th>Screening not completed due to:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Numbers of eligible women who presented to the service
Numbers Screened
% women screened
Numbers Domestic violence identified i.e answered yes to questions 1 and/or 2
Numbers Assistance accepted when domestic violence identified
Numbers Police notifications
Numbers DoCS reports
Numbers Other referrals
Numbers Presence of partner
Numbers Presence of others
Numbers Woman refused to answer questions
Numbers Lack of privacy
Numbers Women too unwell to screen
Numbers Not stated

Does November seem a generally typical month, or is it noticeably different in any way? Please comment.
### Acute intoxication states from commonly used drugs

<table>
<thead>
<tr>
<th>Class of drug</th>
<th>Intoxication</th>
<th>Overdose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Opioids</strong></td>
<td>Miosis</td>
<td>Unconscious</td>
</tr>
<tr>
<td>(eg, heroin, morphine)</td>
<td>Itching</td>
<td>Respiratory depression</td>
</tr>
<tr>
<td></td>
<td>Sedation/somnolence</td>
<td>Pinpoint pupils</td>
</tr>
<tr>
<td></td>
<td>Lowered blood pressure</td>
<td>Hypotension</td>
</tr>
<tr>
<td></td>
<td>Slowed pulse</td>
<td>Bradycardia</td>
</tr>
<tr>
<td></td>
<td>Hypoventilation</td>
<td>Pulmonary oedema</td>
</tr>
<tr>
<td><strong>Stimulants</strong></td>
<td>Hyperactivity</td>
<td>Panic</td>
</tr>
<tr>
<td>(eg, cocaine, amphetamines)</td>
<td>Restlessness</td>
<td>Acute paranoid psychosis</td>
</tr>
<tr>
<td></td>
<td>Agitation</td>
<td>Seizures</td>
</tr>
<tr>
<td></td>
<td>Anxiety/nervousness</td>
<td>Cardiac arrhythmias</td>
</tr>
<tr>
<td></td>
<td>Mydriasis</td>
<td>Myocardial ischemia (rarely infarct)</td>
</tr>
<tr>
<td></td>
<td>Elevated blood pressure</td>
<td>Hypertensive crisis</td>
</tr>
<tr>
<td></td>
<td>Increased pulse</td>
<td>Cerebrovascular accidents</td>
</tr>
<tr>
<td></td>
<td>Raised temperature</td>
<td>Hyperpyrexia</td>
</tr>
<tr>
<td></td>
<td>Sweating</td>
<td>Dehydration</td>
</tr>
<tr>
<td></td>
<td>Tremor</td>
<td></td>
</tr>
<tr>
<td><strong>Benzodiazepines</strong></td>
<td>Disinhibition</td>
<td>Stupor/coma</td>
</tr>
<tr>
<td>(eg, diazepam, oxazepam, flunitrazepam)</td>
<td>Sedation</td>
<td>Ataxia</td>
</tr>
<tr>
<td></td>
<td>Drooling</td>
<td>Confusion</td>
</tr>
<tr>
<td></td>
<td>Incoordination</td>
<td>Respiratory depression</td>
</tr>
<tr>
<td></td>
<td>Slurred speech</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lowered blood pressure</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dizziness</td>
<td></td>
</tr>
<tr>
<td><strong>Cannabis</strong></td>
<td>Relaxation</td>
<td>Paranoid psychosis</td>
</tr>
<tr>
<td></td>
<td>Decreased concentration</td>
<td>Confusion</td>
</tr>
<tr>
<td></td>
<td>Decreased psychomotor performance</td>
<td>Agitation</td>
</tr>
<tr>
<td></td>
<td>Impaired balance</td>
<td>Anxiety/panic</td>
</tr>
<tr>
<td></td>
<td>Conjunctival injection</td>
<td>Hallucinations</td>
</tr>
<tr>
<td><strong>Alcohol</strong></td>
<td>Relaxation</td>
<td>Disorientation/confusion</td>
</tr>
<tr>
<td></td>
<td>Disinhibition</td>
<td>Respiratory depression</td>
</tr>
<tr>
<td></td>
<td>Impaired coordination</td>
<td>Loss of consciousness</td>
</tr>
<tr>
<td></td>
<td>Impaired judgement</td>
<td>Loss of bladder control</td>
</tr>
<tr>
<td></td>
<td>Decreased concentration</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Slurred speech</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ataxia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vomiting</td>
<td></td>
</tr>
</tbody>
</table>
Withdrawal states from commonly used drugs

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Onset</th>
<th>Duration</th>
<th>Symptoms of withdrawal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioids</td>
<td>8–12 hours</td>
<td>Peaks 2–4 days, ceases 7–10 days</td>
<td>Anxiety, muscle tension, muscle and bone ache, muscle cramps, sleep disturbance, sweating, hot and cold flushes, piloerection, yawning, lacrimation, rhinorrhoea, abdominal cramps, nausea, vomiting, diarrhoea, palpitations, elevated blood pressure and pulse, dilated pupils</td>
</tr>
<tr>
<td>Stimulants</td>
<td>8–36 hours</td>
<td>Several days, occasionally 2–3 weeks</td>
<td>Lethargy, depression, irritability, hyperphagia, anhedonia, dysphoria, desire for sleep increased</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>1–10 days (depending on half-life)</td>
<td>3–6 weeks (may be longer)</td>
<td>Anxiety, insomnia, muscle aching and twitching, perceptual changes, feelings of unreality, depersonalisation, seizures</td>
</tr>
<tr>
<td>Cannabis</td>
<td>Usually days</td>
<td>Weeks</td>
<td>Irritability, anxiety, insomnia, anorexia, sweating, muscle spasms, headaches</td>
</tr>
<tr>
<td>Alcohol</td>
<td>As blood alcohol level falls, depends on rate of fall and hours after last drink</td>
<td>5–7 days</td>
<td>Anxiety, agitation, sweating, tremor, nausea, vomiting, abdominal cramps, diarrhoea, anorexia, craving, insomnia, elevated blood pressure and pulse, temperature, headache, seizures, confusion, perceptual distortions, disorientation, hallucinations, hyperpyrexia</td>
</tr>
</tbody>
</table>
Assessment module for opioid treatment program induction

This assessment module is designed to document the key stages of the assessment of a patient being considered for methadone maintenance treatment. The form provides for a structured assessment that covers all the essential stages of information gathering, examination and counselling. It is designed to be used by ticking boxes to record key findings and writing the details in the lines nearby.

The 10-page assessment module can be photocopied for use in any clinical setting.
2. Presentation

Presenting date / /  

Reason for presentation at this time

Assessed by  
(list all)

Referred by

3. Drug use history

Brief outline

Drug use summary

<table>
<thead>
<tr>
<th>Drugs used</th>
<th>Days used in last month</th>
<th>Amount/ times daily</th>
<th>Route</th>
<th>Date, time of last use</th>
<th>Age at start of regular use</th>
<th>Longest abstinence, date</th>
</tr>
</thead>
</table>
4. Previous alcohol/drug-use treatment

<table>
<thead>
<tr>
<th>Treatment</th>
<th>When</th>
<th>Duration</th>
<th>Treatment provider / comments</th>
</tr>
</thead>
</table>

- Inpatient detoxification
- Outpatient detoxification
- Residential rehabilitation
- Counselling/psychotherapy
- Narcotics Anonymous
- Methadone treatment
- Buprenorphine treatment
- Other

5. Problems related to drug use

<table>
<thead>
<tr>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relationship</td>
</tr>
<tr>
<td>Family</td>
</tr>
<tr>
<td>Social</td>
</tr>
<tr>
<td>Medical</td>
</tr>
<tr>
<td>Psychological</td>
</tr>
<tr>
<td>Financial</td>
</tr>
<tr>
<td>Legal</td>
</tr>
<tr>
<td>Overdoses</td>
</tr>
</tbody>
</table>
6. Medical history

Gastrointestinal  (infectious hepatitis, liver disease, peptic ulceration, bowel habit, other current symptoms)

Cardiovascular  (hypertension, endocarditis, other current symptoms)

Respiratory  (asthma, bronchitis, other current symptoms)

Neurological  (seizures, head injury, other current symptoms)

Genito-urinary  (pregnancy, STDs, sexual dysfunction, menstrual dysfunction, other current symptoms, contraception)

Endocrine  (diabetes, thyroid disease, other current symptoms)

Other  (chronic pain, musculoskeletal [trauma, arthritis], dermatological)

Prescribed medications

Key conditions
(complete after taking history)

- Pregnant
- HIV positive
- Hepatitis C positive
- Chronic hepatitis B infection
- Hepatitis B vaccination
- Liver disease
- Cardiovascular disease
- Respiratory disease
- Renal disease
- Chronic pain
- Drug allergies
- Oral contraceptive use
7. Infectious risk behaviour

<table>
<thead>
<tr>
<th>Frequency of needle sharing in last three months (per day, week or month)</th>
<th>Use of bleach to clean needles before re-use (always, sometimes, never, doesn’t re-use needles)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Needle sharing partners in last three months</th>
<th>Number of sexual partners for unprotected penetrative sex in last three months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number using needle before:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Number using needle after:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

8. Psychiatric history

<table>
<thead>
<tr>
<th>Details</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td></td>
</tr>
<tr>
<td>Mania</td>
<td></td>
</tr>
<tr>
<td>Psychosis</td>
<td></td>
</tr>
<tr>
<td>Suicide attempts</td>
<td></td>
</tr>
<tr>
<td>Previous psychiatric treatment</td>
<td></td>
</tr>
</tbody>
</table>

9. Family history

<table>
<thead>
<tr>
<th>Details</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychiatric disorders</td>
<td></td>
</tr>
<tr>
<td>Medical conditions</td>
<td></td>
</tr>
<tr>
<td>Drug or alcohol problems</td>
<td></td>
</tr>
<tr>
<td>Problem family relationships</td>
<td></td>
</tr>
<tr>
<td>Domestic violence issues</td>
<td></td>
</tr>
</tbody>
</table>
10. **Personal/social history**

**Current stressors** (losses, problems with relationships, or financial, legal, employment or accommodation difficulties)

<table>
<thead>
<tr>
<th>Current stressors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Losses, problems with relationships</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

**Past significant life events**

- History of abuse
- Loss of significant others
- Other traumatic events

**Current social situation and significant relationships**

- Single
- Married/defacto relationship
- Separated or divorced
- Supportive friends
- Abusive partner
- Children, separated
- Supportive relatives
- Drug-using cohabitants
- Dependent children

**Note:** Complete NSW Health routine screening for domestic violence for all women.

**Formal qualifications and skills**

<table>
<thead>
<tr>
<th>Formal qualifications and skills</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

**Income and employment**

<table>
<thead>
<tr>
<th>Income and employment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

**Legal history**

- Currently facing charges
- Past conviction
- Time in gaol
11. Mental state examination

General appearance and behaviour (attire, grooming, movements [agitated, retarded], speech, attitude to examiner)

Affect and mood (affect — quality, range, appropriateness; mood)

Thought (tempo, form, content, delusions, suicidal or homicidal ideas)

Perception (hallucinations, illusions, perceptual distortions)

Cognition (orientation, memory, attention, concentration)

Insight
12. Physical examination

<table>
<thead>
<tr>
<th>BP</th>
<th>Pulse</th>
<th>Temp</th>
<th>Weight</th>
</tr>
</thead>
</table>

Head and neck

Cardiovascular

Respiratory

Abdomen

Lymph nodes

Central nervous system

Periphery

Evidence of injecting drug use (indicate where)

- Needle marks
- Venous scarring
- Phlebitis

Evidence of intoxication

- Opioids (pinpoint pupils, sedation, low blood pressure, slowed pulse, itching/scratching)
- Benzodiazepines (slurred speech, ataxia, sedation, nystagmus, low blood pressure, drooling, disinhibition)
- Amphetamines (hyperactive, disinhibited, dilated pupils, high blood pressure, tremor, tachycardia)
- Alcohol (ataxia, slurred speech, disinhibited, low blood pressure, smells of alcohol)
Evidence of opioid withdrawal

- History (muscle tension/pain, bone aches, cramps, nausea, sleep disturbances, coldness, shivering, abdominal cramps, palpitations)

- Examination (lacrimation, rhinorrhoea, yawning, gooseflesh, piloerection, sweating, dilated pupils, elevated BP and pulse, vomiting, diarrhoea, muscle spasm, twitching)

Evidence of opioid dependence

- Tolerance
- Withdrawal syndrome
- Opioids used in larger amounts or for longer periods than was intended
- Persistent desire or unsuccessful attempts to reduce opioid use
- Great deal of time spent in obtaining, using and recovering from the use of opioids
- Important social, occupational or recreational activities are reduced because of opioid use
- Opioid use is continued despite knowledge that it causes or exacerbates physical or psychological problems

13. Evidence of opioid dependence

14. Management plan

Suitability for methadone or buprenorphine maintenance treatment

- Opioid dependent
- Not primarily dependent on another drug
- Aged 16 or more
- Competent to consent

- Suitable for methadone maintenance treatment.
- Suitable for buprenorphine maintenance treatment.
- Not suitable for methadone maintenance treatment. Alternative treatment plan:
Investigations

- Urine test for opioids
- Hepatitis serology
- HIV test
- Liver function tests

Patient information given

- Treatment aims
- Methadone/buprenorphine effects and side effects

Warnings

- Overdose
- Control of vehicles

Patient routine obligations

- Appointments/collections
- Report use of other drugs
- Report withdrawal symptoms
- Provide urine tests
- Attend counselling

Consequences of non-compliance

Involuntary discharge conditions

- Violence
- Diversion of doses
- Failure to collect doses
- Drug dealing

Other

- Support services available
- Review and appeal process
- Reducing infectious risk behaviour

Initial treatment plan

- Methadone maintenance
- Buprenorphine maintenance

Starting date and dose:

Early monitoring arrangements:

Initial harm reduction actions:

Case management arrangements:

Checklist

- Printed information supplied
- Informed consent to treatment obtained
- NSW Health treatment agreement signed
- Patient requested to obtain four ID photos
- PSB application to prescribe completed
- Physical description documented
- Treatment sheet with doctor’s instructions or prescription
K Example of written patient information for induction to treatment

This example of written patient information is from South Western Sydney Area Health Service Drug Health Services. As well as giving a copy to the patient, the patient is asked to sign a copy that is kept in the medical record.
Methadone and buprenorphine patient information

You are encouraged to discuss any of these issues at any time during your treatment with your case manager or prescriber.

**Pregnancy**

Buprenorphine is not licensed for use during pregnancy and precautions (contraception) against becoming pregnant should be taken. If you become pregnant during your time on buprenorphine you need to let your prescriber/case manager know as soon as possible. If you think you may be pregnant, please ask the clinic staff to arrange a test.

**Driving**

It is your responsibility to notify the Roads and Traffic Authority and your insurers that you are on methadone or buprenorphine. You should not drive or operate heavy machinery during the first 3–4 days of starting either of these medications or following dose adjustments since they may cause drowsiness.

**Buprenorphine and precipitated withdrawal**

Taking buprenorphine while you are still affected by other opioid drugs, such as heroin or methadone, can lead to severe withdrawal discomfort (“hanging out”). You should never take buprenorphine within at least 6–8 hours of last using heroin or 24 hours of last using methadone.

**Telling other prescribers and health care workers about your medication**

You should tell any doctor you see that you are on methadone or buprenorphine, since other medication may affect how methadone or buprenorphine work and it may affect the choice of treatment you receive. Buprenorphine can interfere in the action of many major painkillers and you should tell doctors and ambulance staff you are taking it if involved in an accident.

**Suddenly stopping**

Stopping either methadone or buprenorphine suddenly can be associated with physical discomfort, not unlike the “hanging out” feelings people get when they stop heroin. You should always reduce your methadone or buprenorphine gradually over days or weeks and only stop after consulting with your prescriber or case manager.

**Overdose**

You should take your medication as prescribed. Mixing with alcohol or other drugs (especially heroin or benzodiazepines, such as valium) risks overdose.

**Behaviour**

Abusive or aggressive behaviour is not tolerated at this clinic and such behaviour may result in your treatment being stopped or transferred.

**Attendance and appointments**

You should present for treatment daily for your methadone dose and/or as required for buprenorphine dose. You must attend your regular case reviews with your case manager and script reviews with your prescriber.

If you do not attend the appointments with your case manager or prescriber your dose may be withheld since it is unsafe to continue providing opioid medications without regular review.

It is also expected that you will leave the clinic (including hospital grounds) or pharmacy as soon as you have completed dosing or an appointment.

**Urine tests**

You will be asked to provide urine samples for routine drug screens. These are to monitor your progress in treatment and to support the clinic in planning your treatment including the provision of takeaway doses from pharmacies.
Dosing
Your medication is supervised to prevent diversion. Diversion of your drugs to other people may lead to fatal overdose if consumed by those with no tolerance. Diversion of your dose will be considered a serious problem and may lead to dismissal from the program.

Drug dealing
Drug dealing is not tolerated on the hospital grounds and may result in dismissal from the program.

Intoxication
It is dangerous to consume methadone with other drugs especially alcohol, opioids and benzodiazepines. If you present intoxicated with other drugs you may be refused dosing for your own safety.

Transfer to community dosing
Once stabilised on methadone or buprenorphine your dosing point will be changed to a conveniently located community pharmacy. For most people this occurs after 1–3 months of treatment at the public clinic.

Take home doses
Take home doses are not provided from public clinics. Once stable on dosing at a pharmacy you may be given methadone take home doses in line with State guidelines (please ask your case worker for a copy of these if you wish to see them).

Methadone, even in a small dose, can be lethal if consumed by people who are not used to it (particularly children). If you are given takeaway doses you must store them in safe place that cannot be accessed by other people (particularly children) and only take them as prescribed.

I have had the above information regarding my treatment explained to me and have had the chance to ask any questions. I agree to participate in my treatment as is required.

Client's Name:  
Prescriber's Name:  
Signature:  
Signature:  
Date:  
Date:
**L Suitability for takeaway doses assessment form**

**Patient ID:** ________________________  **Date:** ________________________

**Prescriber REF:** ________________________

**Notes:**
1. Eligibility for takeaway doses should be reassessed at each regular review.
2. Guidance on the interpretation of these criteria is contained in *NSW Health Opioid Treatment Program: clinical guidelines for methadone and buprenorphine treatment of opioid dependence*.

All prescribers must complete **Stage one** of this form at commencement of takeaway treatment and at every treatment review. **Stage two** of this form must be completed if the level of risk presented by the patient is high (see explanation below). Completing Stage two of this form is also recommended if the level of risk presented by the patient is medium (see explanation below).

**Level of risk**  **Explanation**

**High**

If the answer is “Yes, in the last 3 months” to any of the questions in Stage one, or you are inexperienced in providing takeaway doses the **stage two checklist must also be completed**.

**Medium**

If the answer is “Yes, in the last 12 months” to any of the questions in Stage one, the **stage two checklist is recommended**.

**Low**

If the answer is “No” to all the questions in Stage one and:
- there are recent favourable reports from dosing points
- only single takeaway doses will be or are being provided (ie, two or three a week)
- the patient’s dose is in the low range (<100 mg)
- the patient has regular employment, education or family responsibilities

less scrutiny is needed but takeaway doses should always be prescribed with caution.

<table>
<thead>
<tr>
<th>Stage one questions</th>
<th>Yes, in the last 3 months</th>
<th>Yes, in the last 12 months</th>
<th>No</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is the patient new to treatment?</td>
<td></td>
<td></td>
<td></td>
<td>Takeaway doses not allowed except under exceptional circumstances if patient is in first 3 months of treatment.</td>
</tr>
<tr>
<td>Is there evidence of illicit drug use (track marks, urine toxicology, intoxication)?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Compromised parenting skills or DOCS involvement with child/children?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Legal issues?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of high doses (&gt;150 mg daily) or more than 4 takeaway doses per week?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chaotic or self-harming behaviours?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

If yes to any of the above in the last 3 months, Stage two must be completed.
If yes to any of the above in the last 12 months, Stage two is recommended.
### Stage two

<table>
<thead>
<tr>
<th>Absolute contraindications to providing takeaway doses</th>
<th>Yes</th>
<th>No</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repeated intoxication on presentation for dosing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parenting concerns/DOCS involvement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current chaotic and unpredictable behaviour</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Assessed as high risk of self-harm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hazardous use of drugs including alcohol and benzodiazepines</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**If “yes” to any of the above takeaway doses are not be provided.** This decision can be reviewed at next patient medical review to determine if a patient’s eligibility has changed.

<table>
<thead>
<tr>
<th>Drug use</th>
<th>Yes</th>
<th>No</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>The patient has diverted doses within the last 3 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>There is evidence of continued illicit substance use in the last 3 months (urine testing, injection)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**If “yes” to any of the above clinical judgment is to be used to determine the appropriateness of takeaway doses.**

<table>
<thead>
<tr>
<th>Psychosocial stability</th>
<th>Yes</th>
<th>No</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient attends clinic appointments and complies with treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient demonstrates acceptable behaviour (ie, not aggressive)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient has evidence of employment/educational/family activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient reports stable accommodation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stable mental and physical health</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**If “no” to any of the above clinical judgment is to be used to determine the appropriateness of takeaway doses.**

<table>
<thead>
<tr>
<th>Access issues (Evidence should be cited)</th>
<th>Yes</th>
<th>No</th>
<th>Comments, evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do work, education, parenting commitments or travel hardship interfere with daily attendance at dosing site?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Access issues alone are insufficient reason to prescribe takeaway doses, although they may contribute to the determination of the frequency of takeaway doses.

<table>
<thead>
<tr>
<th>Children at risk of harm: to be completed if children aged 0–16 live in the patient’s household</th>
<th>Yes</th>
<th>No</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are there any observations you have made in the last three months that may indicate that parenting is compromised?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have you sighted or examined the child/children the patient resides with in the last three months?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Child safety statement**

I have informed the patient of the requirement to keep their medication in a safe locked container away from the reach of children. I have reinforced that the medication is dangerous, if others particularly children ingest it.

Not Applicable

Prescriber’s signature: ___________________________ Date: ___________________________
NSW Health forms used in the administration of the Opioid Treatment Program

<table>
<thead>
<tr>
<th>Form</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application to prescribe pharmacotherapies</td>
<td>To register as a prescriber of methadone or buprenorphine treatment</td>
</tr>
<tr>
<td>Application for authority to prescribe methadone</td>
<td>To enrol a new patient in methadone maintenance treatment</td>
</tr>
<tr>
<td>Application for authority to prescribe buprenorphine</td>
<td>To enrol a new patient in buprenorphine maintenance treatment</td>
</tr>
<tr>
<td>Treatment Agreement</td>
<td>Must be signed by all patients in the Opioid Treatment Program in NSW</td>
</tr>
<tr>
<td>Application form for methadone doses above 200 mg</td>
<td>To secure approval to prescribe a daily methadone dose above 200 mg</td>
</tr>
<tr>
<td>Application form for buprenorphine doses above 32 mg</td>
<td>To secure approval to prescribe a daily buprenorphine dose above 32 mg</td>
</tr>
<tr>
<td>Treatment exit</td>
<td>To exit a patient from an opioid treatment program</td>
</tr>
</tbody>
</table>
Dear Sir/Madam

Re: Approval to Prescribe Pharmacotherapies

I wish to formally apply under the statutory requirements of the NSW Poisons and Therapeutic Goods Act 1966, to be approved as a pharmacotherapies prescriber for the purpose of treating opioid dependent individuals.

I understand that as a prerequisite for approval I will need to successfully complete the Pharmacotherapies Accreditation Course and demonstrate clinical competence in pharmacotherapies treatment.

I am interested in attending the Pharmacotherapies Accreditation Course on: ________________________, at __________________________________________

(date)     (location)

Attached, please find my Curriculum Vitae, which details my qualifications, employment history and other information relevant to my application.

My Provider number is:____________________ My Prescriber number is: _________________________

My NSW Medical Board Registration Number is: ________________________________________________

I understand that my application and supporting papers will be forwarded to the Pharmacotherapy Credentialling Subcommittee, and my name will be passed to the Pharmaceutical Services Branch and the Health Care Complaints Commission for advice as to any matters under investigation, to the NSW Medical Board (and, if appropriate, to equivalent bodies in other states) for advice as to any relevant matters relating to my professional conduct, performance or health.

If you have any questions, I can be contacted by telephone on:________________________________________

Please forward correspondence regarding this application to:________________________________________________________________________________________

(street address)

(suburb and postcode)

To enable the Department to better understand our treatment program, please complete the following:

Tick the box(es) that best describes your current title/qualification:

☐ Registrar, ☐ General Practitioner, ☐ Physician, ☐ Psychiatrist, ☐ CMO ☐ VMO,

☐ Fellow Chapter Addiction Medicine, ☐ OTHER____________________________________

Tick the box(es) that best describes your current work setting:

☐ Public clinic, ☐ Private clinic, ☐ General Practice

Yours sincerely

____________________  _____________________      ________________________________
(signature)   (printed name)           (date)
**APPLICATION FOR AUTHORITY TO PRESCRIBE METHADONE**

*(IN ACCORDANCE WITH SECTION 29 AND CLAUSE 157 UNDER THE POISONS AND THERAPEUTIC GOODS ACT 1966)*

**REFER TO INSTRUCTIONS ON THE REVERSE SIDE.**

**PLEASE USE BLOCK LETTERS.**

<table>
<thead>
<tr>
<th>(P.S.B.) Ref. No.:</th>
<th>ST.DATE:</th>
<th>TRANSFER:</th>
<th>[OFFICE USE ONLY]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Y / N</td>
<td></td>
</tr>
</tbody>
</table>

1. **SURNAME:**

2. **GIVEN NAMES:**

3. **ALSO KNOWN AS:**

4. **ADDRESS:**

5. **SUBURB:** POSTCODE: ___ ___ ___

6. **DATE OF BIRTH:** ___ / ___ / ___

7. **GENDER:**

   - M
   - F

8. **IDENTIFICATION VERIFIED (see over):**

   - Y
   - N

9. **Is the client CURRENTLY on a methadone or buprenorphine program in NSW?** *(Tick one box only)*

   - Y, methadone
   - N ➔ GO TO Q.19

   - Y, buprenorphine
   - N ➔ GO TO Q.19

10. **Are you the client’s CURRENT prescriber?**

    - Y ➔ GO TO Q.15
    - N ➔ GO TO Q.15

11. **Indicate below the purpose of this application: (Tick one box only)**

    - To INCREASE the MAXIMUM AUTHORISED DOSE of methadone ➔ GO TO Q.33

    - To TRANSFER the client from BUPRENOPIHINE TREATMENT ➔ GO TO Q.12

   **Note:** For transfers from buprenorphine to methadone treatment with the same prescriber, do not lodge an ‘Exit from Methadone/ Buprenorphine Treatment’ form for current buprenorphine program

12. **Was buprenorphine used primarily for WITHDRAWAL or MAINTENANCE?** *(Tick one box only)*

    - withdrawal
    - maintenance

13. **Date of LAST DOSE of buprenorphine:**

    ___ ___ / ___ ___ / ___ ___

14. **LAST DOSE of buprenorphine:** ___ ___ mg ➔ GO TO Q.30

15. **Specify the NAME of the client’s CURRENT prescriber.**

16. **Is the client TRANSFERRING from GAOL?**

    - Y
    - N ➔ GO TO Q.30

17. **Date of LAST DOSE dispensed on GAOL PRESCRIPTION, including any takeaways:**

    ___ ___ / ___ ___ / ___ ___

18. **LAST DOSE:** ___ ___ mg ➔ GO TO Q.30

19. **Has the client PREVIOUSLY been on a methadone or buprenorphine program in NSW?**

    - Y, specify last prescriber ➔ GO TO Q.30
    - N

20. **Is the client TRANSFERRING from ANOTHER STATE or TERRITORY?**

    - Y, specify (e.g. Vic.) ➔ GO TO Q.30
    - N

   **If YES,** attach statement signed by interstate prescriber showing dose and date of last dose (incl. takeaways)

21. **Is the client of ABORIGINAL or TORRES STRAIT ISLANDER origin?**

    - 1 Yes, Aboriginal
    - 2 Yes, Torres Strait Islander
    - 3 Yes, both Aboriginal and Torres Strait Islander
    - 4 No

22. **What is the client’s MAIN SOURCE of INCOME?** *(Tick one box only)*

    - 01 full-time employment
    - 02 part-time employment
    - 03 temporary benefit, e.g. unemployment
    - 04 pension, e.g. aged, disability
    - 05 student allowance
    - 06 dependent on others
    - 07 retirement fund
    - 98 other

---

New South Wales Opioid Treatment Program
<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>In which COUNTRY was the client born?</td>
<td></td>
</tr>
<tr>
<td>Australia</td>
<td></td>
</tr>
<tr>
<td>other, specify</td>
<td></td>
</tr>
<tr>
<td>Primary opioid drug of dependence</td>
<td></td>
</tr>
<tr>
<td>heroin</td>
<td></td>
</tr>
<tr>
<td>other, specify</td>
<td></td>
</tr>
<tr>
<td>Drug(s), other than opioids, does the client perceive as a health concern?</td>
<td></td>
</tr>
<tr>
<td>990 none</td>
<td></td>
</tr>
<tr>
<td>010 alcohol</td>
<td></td>
</tr>
<tr>
<td>030 cannabis</td>
<td></td>
</tr>
<tr>
<td>040 sedatives and hypnotics, e.g. benzodiazepines</td>
<td></td>
</tr>
<tr>
<td>050 stimulants and related synthetic drugs, e.g. amphetamines, cocaine, ecstasy (MDMA), PMA</td>
<td></td>
</tr>
<tr>
<td>other, specify</td>
<td></td>
</tr>
<tr>
<td>Treatment for opioid dependence has previously been given</td>
<td></td>
</tr>
<tr>
<td>06 none</td>
<td></td>
</tr>
<tr>
<td>01 assessment only</td>
<td></td>
</tr>
<tr>
<td>07 counselling</td>
<td></td>
</tr>
<tr>
<td>02 detoxification/withdrawal</td>
<td></td>
</tr>
<tr>
<td>03 residential rehabilitation activities</td>
<td></td>
</tr>
<tr>
<td>08 day program rehabilitation activities</td>
<td></td>
</tr>
<tr>
<td>04 maintenance pharmacotherapy, e.g. naltrexone</td>
<td></td>
</tr>
<tr>
<td>other, specify</td>
<td></td>
</tr>
<tr>
<td>Is the client pregnant?</td>
<td></td>
</tr>
<tr>
<td>Y</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td></td>
</tr>
<tr>
<td>not applicable</td>
<td></td>
</tr>
<tr>
<td>Is the client or the client's opioid-using partner HIV positive?</td>
<td></td>
</tr>
<tr>
<td>Y</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td></td>
</tr>
<tr>
<td>not stated</td>
<td></td>
</tr>
<tr>
<td>Client aged 16 years to under 18 years, write below</td>
<td></td>
</tr>
<tr>
<td>the name of the approved methadone prescriber providing second opinion</td>
<td></td>
</tr>
<tr>
<td>Report must be attached</td>
<td></td>
</tr>
<tr>
<td>Has the treatment agreement been signed by the client? (see 'Instructions')</td>
<td></td>
</tr>
<tr>
<td>Y</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td></td>
</tr>
<tr>
<td>Proposed starting dose of methadone (determined in accord with clinical assessment)</td>
<td></td>
</tr>
<tr>
<td>mg</td>
<td></td>
</tr>
<tr>
<td>Proposed starting date</td>
<td></td>
</tr>
<tr>
<td>mm/dd/yyyy</td>
<td></td>
</tr>
<tr>
<td>Expected maximum dose of methadone</td>
<td></td>
</tr>
<tr>
<td>mg</td>
<td></td>
</tr>
<tr>
<td>Proposed administration point</td>
<td></td>
</tr>
<tr>
<td>[OFFICE USE ONLY: ]</td>
<td></td>
</tr>
<tr>
<td>I, the undersigned, declare that the client's opioid dependence</td>
<td></td>
</tr>
<tr>
<td>has established using current best practice*, and that the client</td>
<td></td>
</tr>
<tr>
<td>has been assessed suitable for methadone treatment. (* see 'Instructions')</td>
<td></td>
</tr>
<tr>
<td>Prescriber's signature</td>
<td></td>
</tr>
<tr>
<td>Prescriber's name</td>
<td></td>
</tr>
<tr>
<td>[OFFICE USE ONLY: ]</td>
<td></td>
</tr>
<tr>
<td>Address</td>
<td></td>
</tr>
<tr>
<td>Date</td>
<td></td>
</tr>
<tr>
<td>Ph</td>
<td></td>
</tr>
<tr>
<td>Fax</td>
<td></td>
</tr>
</tbody>
</table>

**TO BE COMPLETED BY CLIENT**

I hereby declare that I have not knowingly supplied any false particulars above and that I am (*NOT CURRENTLY ON ANY OTHER TRANSFERRING FROM ANOTHER*) methadone or buprenorphine program. I have been explained the nature of methadone treatment and the potential side effects of methadone, and I consent to being treated with methadone. I also understand that the particulars I have supplied may be stored confidentially on a central register.

Name: 

Signature: 

Date: 

*Cross out whichever does not apply
### Client’s Name: ___________________________ (prescriber to complete)

22. In which COUNTRY was the client born?
   - [ ] 1100 Australia
   - [ ] other, specify ___________________________

23. What is the client’s PRIMARY opioid drug of dependence?
   - [ ] heroin
   - [ ] other, specify ___________________________

24. What DRUG(S), OTHER THAN opioids, does the client perceive as being a health concern? (Tick the appropriate box(es))
   - [ ] 990 none
   - [ ] 010 alcohol
   - [ ] 030 cannabis
   - [ ] 040 sedatives and hypnotics, e.g. benzodiazepines
   - [ ] 050 stimulants and related synthetic drugs, e.g. amphetamines, cocaine, Ecstasy (MDMA), PMA
   - [ ] other, specify ___________________________

25. What TREATMENT for OPIOID DEPENDENCE has PREVIOUSLY been given (other than buprenorphine or methadone maintenance/withdrawal treatment)? (Tick the appropriate box(es))
   - [ ] 06 none
   - [ ] 01 assessment only
   - [ ] 07 counselling
   - [ ] 02 detoxification/withdrawal
   - [ ] 03 residential rehabilitation activities
   - [ ] 08 day program rehabilitation activities
   - [ ] 04 maintenance pharmacotherapy, e.g. naltrexone
   - [ ] 98 other, specify ___________________________

26. Is the client or the client’s opioid-using partner HIV positive?
   - [ ] Y
   - [ ] N
   - [ ] not stated

27. If client is aged 16 YEARS TO UNDER 18 YEARS, write below the name of the APPROVED BUPRENORPHINE PRESCRIBER providing SECOND OPINION. Report must be attached.

28. Is buprenorphine to be used primarily for WITHDRAWAL or MAINTENANCE? (Tick one box only)
   - [ ] withdrawal
   - [ ] maintenance

29. Has the TREATMENT AGREEMENT been signed by the client? (see 'Instructions')
   - [ ] Y
   - [ ] N

30. Proposed STARTING DOSE of buprenorphine (determined in accord with clinical assessment): ______ mg

31. Proposed STARTING DATE: ______ / ______ / ______

32. Expected MAXIMUM DOSE of buprenorphine: ______ mg

33. Proposed ADMINISTRATION POINT:

[OFFICE USE ONLY: ___________________________]

I, the undersigned, declare that the client's opioid dependence has been established using CURRENT BEST PRACTICE*, and that the client has been assessed suitable for BUPRENORPHINE treatment. (*see 'Instructions')

Prescriber’s Signature: ___________________________

Prescriber’s Name: ___________________________

[OFFICE USE ONLY: ___________________________]

Address: _______________________________________

Date: _________________________________________

Ph: __________________ Fax: ____________________

**TO BE COMPLETED BY CLIENT**

I hereby declare that I have not knowingly supplied any false particulars above and that I am (NOT CURRENTLY ON ANY OTHER /TRANSFERRING FROM ANOTHER) buprenorphine or methadone program. I have been explained the nature of buprenorphine treatment and the potential side effects of buprenorphine, and I consent to being treated with buprenorphine. I also understand that the particulars I have supplied may be stored confidentially on a central register.

Name: _______________________________________

Signature: ____________________________________

Date: _________________________________________

*Cross out whichever does not apply
Treatment Agreement

Conditions of methadone/buprenorphine treatment

CLIENTS’ RESPONSIBILITIES

Drug use
Clients work with their prescriber and case manager to make the life changes necessary to stop using other opiates and other illicit drugs, including the misuse of legal drugs.

Behaviour
Clients assist in maintaining a safe environment for health care workers and other clients, by not being verbally or physically threatening or violent, not damaging property, and keeping the environment free from smoke and free from unrestrained animals.

Clients do not contribute to crowding around clinics and dispensing points by bringing friends or associates to clinician's appointments or the dispensary unnecessarily. In addition, that clients do not remain around the premises for longer than necessary.

Clients cooperate with the treatment team, or clearly and respectfully communicate to the treatment team the reasons behind the decision not to cooperate.

Clients do not sell or offer drugs, including doing so in the vicinity of the clinic/pharmacy.

Appointments/service rules
Clients adhere to the rules of the methadone/buprenorphine program they are part of.

Clients attend appointments as organised, or inform the worker if they need to cancel.

Clients provide urine specimens as requested.

Clients have their methadone/buprenorphine dose at the dispensing point unless it is provided as a takeaway dose.

Takeaway doses
It is the client’s responsibility to adhere to takeaway policies and acknowledge that any misuse of takeaways may result in the takeaway privilege being revoked. Take away doses are not a right of all clients on methadone/buprenorphine treatment. Takeaway doses may be provided, at the discretion of the prescriber, on the basis of need, suitability and stability. It is illegal to sell or give takeaway doses to anyone.

Clients will not sell or give any takeaway doses away.

Clients will not inject takeaway doses.

Clients must ensure that takeaway doses are stored safely so the methadone/buprenorphine dose is not accessible to children or others.

Urine testing
Clients will be required to provided urine tests randomly at the discretion of the treatment team. If people are unable to provide a sample on the day it should be provided prior to dosing on the following day.

Treatment plans
All clients will participate in the development of a treatment plan which is made in collaboration with the prescriber, case manager, and pharmacist. The Treatment Plan will set short, medium and long term goals for treatment. These will include health progress, life style issues, educational and training needs and family involvement (where appropriate).

CLIENTS RIGHTS

• To receive health care given with consideration and respect, without bias or discrimination, thereby recognising personal dignity at all times.

• To be assured of privacy at interview, and examination and that any further discussion or consultation is conducted with discretion and confidentiality.

• To expect all communications and records pertaining to your care will be treated as confidential and that, in most cases, access to such records will be made available in the presence of a nominated a health care professional of your choice.

• To be advised by the attending clinician, in clear, concise terms which you understand, the complete and current information relating to your condition – including treatment, prognosis, risks, side or after effects and any alternate treatment or procedures.

• To expect adequate information to be provided so that you are able to give informed consent for treatment and procedures. You have the right to refuse services from students and involvement in research.

• To be offered the services of a trained interpreter, if required.

• To know the identity, professional status and qualifications of those providing care and to know which person is primarily responsible for your care.

• To seek alternate health care or a second opinion; refuse treatment or withdraw consent at any time, to the extent provided by law.

• To expect reasonable safety in both environment and practices and seek legal advice if it is perceived that harm has occurred as a result of negligence of the service.

• To nominate a family member, friend or advocate to participate in the decisions regarding your health care.

• Information and consultation regarding treatment costs will be given before treatment.

• To complain and be informed of the process for complaints.
SERVICE PROVIDER / CLINICIAN RESPONSIBILITY

It is the responsibility of the team treating the client to:

- Obtain informed consent to methadone/buprenorphine treatment from the patient before he/she commences treatment.
- Develop and document a treatment plan in collaboration with the patient following initial assessment.
- Develop a more detailed treatment plan in collaboration with the patient after 4 weeks in treatment, and review the plan at least every three months.
- Provide competent care.
- Treat clients with dignity, respect, and courtesy.
- Provide services that are free of physical and mental abuse, coercion, harassment, and discrimination.
- To provide services that take into account the cultural, religious, social and ethnic needs, values and beliefs of clients.
- Identify and address any barriers that the patient may have to informed participation in methadone/buprenorphine treatment such as: literacy, non-English speaking, intoxication and disability.
- Provide takeaway doses only after careful assessment of a patients stability and reliability.
- Provide education about overdose risk, particularly the risk of combining other drugs (including alcohol) with methadone/buprenorphine and the strategies to avoid and manage overdose.
- Provide information and strategies to enhance the patient’s capacity to successfully withdraw from methadone/buprenorphine.
- Support a client’s right to make a complaint and have conflicts resolved by:
  - Providing all patients with information on and access to procedures for complaint handling and conflict resolution.
  - Being familiar with complaint procedures and best practice complaint handling.
- An experienced clinician is to review the treatment progress of all patients at least four times a year.

APPEAL MECHANISMS

Clients need to know avenues of appeal for decisions made by providers to significantly change the client’s current arrangements, decline a request to change conditions of treatment by the client (unless these contravene DoH policy or guidelines) or remove the client from the program.

Clients who do not comply with the conditions of methadone/buprenorphine programs in NSW will have their place on the methadone/buprenorphine program reviewed.

The following actions will be taken sequentially when clients do not comply with conditions of the program:

1. A formal warning will be given.
2. A change in conditions of program will occur including removal of takeaway doses and the requirement to attend more frequent appointments.
3. Transfer to a more supervised treatment setting.
4. Withdrawal from the program.

* Certain actions, namely violence or threat of violence against staff or other patients, property damage or theft from the methadone/buprenorphine program, drug dealing on or near treatment premises, and repeated diversion of methadone/buprenorphine may warrant immediate discharge from treatment.

Client

I understand the rights and responsibilities outlined in this agreement and have received the following information:

- NSW Health Methadone overdose card
- NSW Health Methadone Maintenance Treatment Essential Information (or)
- Buprenorphine Patient Information

I understand that this agreement is an interim agreement to be completed after four weeks of treatment.

Signed: .................................................................
Date: .................................................................

Clinician

I understand the rights and responsibilities outlined in this agreement and have provided the following information:

- NSW Health Methadone overdose card
- NSW Health Methadone Maintenance Treatment Essential Information (or)
- Buprenorphine Patient Information

Signed: .................................................................
Date: .................................................................

Treatment plan attached: ☐ yes ☐ no
Application for methadone doses above 200 mg per day

This form will be submitted to the Pharmacotherapy Credentialling Subcommittee for review.

This form should be accompanied by:

1. A second opinion obtained from a prescriber who is a Fellow of the Chapter of Addiction Medicine, or a prescriber of equivalent training and experience as from time to time approved by the PCS.
2. Recent urine drug screen (UDS)

Client’s PSB Number /Patient name…………………………… DOB …………………………………………

Current dose ……….. mg Dose applied for …………………………………… mg

Clinical Details

1. Observations 2-3 hours post dose …………………………………………………………………………………
2. Urine Drug screen. Other drugs present ……………………………………………………………………………
3. Reason for request for increased dose ……………………………………………………………………………
4. Other current medications including dosage ………………………………………………………………………
5. Number of takeaways / week ………………………………………………………………………………………
6. Relevant details of psychosocial situation e.g. chronic pain, psychiatric disorder ……………………………

Has the patient signed a HIC Privacy Release form so that information is available on the number of doctors visited in the last three months? [ ] yes [ ] no (To obtain HIC form ‘phone 1800 420 074)

If this is a chronic pain case, have you addressed the issue of alternative methods of treatment?
[ ] yes [ ] no

Have you submitted a high dose application for this client previously? [ ] yes (date)………. [ ] no

Attachments:
[ ] Second opinion [ ] Recent UDS

Prescriber name……………………………. Signature……………………………………
Mailing address…………………………………………………………………………………………
Phone (w)…………………………………………… Phone (mob)…………………………………
Date ……………………………………………

Subcommittee meetings are scheduled for the second Tuesday of every month, and applications must be received one week prior to the meeting.

Applications should be addressed to: Secretary, PCS, Centre for Drug and Alcohol, NSW Health.
LMB 961 North Sydney, NSW 2059
Fax (02) 9391 9042 Ph: (02) 9391 9244
### Application for buprenorphine doses above 32 mg per day

This form will be submitted to the Pharmacotherapy Credentialling Subcommittee for review.

This form should be accompanied by:

1. A second opinion obtained from a prescriber who is a Fellow of the Chapter of Addiction Medicine, or a prescriber of equivalent training and experience as from time to time approved by the PCS.
2. Recent urine drug screen (UDS)

#### Clinical Details

1. Observations 2-3 hours post dose
2. Urine Drug screen. Other drugs present
3. Reason for request for increased dose
4. Other current medications including dosage
5. Number of takeaways / week
6. Relevant details of psychosocial situation e.g. chronic pain, psychiatric disorder

---

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Client’s PSB Number /Patient name………………………….</td>
<td>DOB ..................................................</td>
</tr>
<tr>
<td>Current dose .......... mg</td>
<td>Dose applied for ........................................... mg</td>
</tr>
</tbody>
</table>

---

Has the patient signed a HIC Privacy Release form so that information is available on the number of doctors visited in the last three months? [ ] yes [ ] no (To obtain HIC form ‘phone 1800 420 074)

If this is a chronic pain case, have you addressed the issue of alternative methods of treatment? [ ] yes [ ] no

Have you submitted a high dose application for this client previously? [ ] yes (date)……….. [ ] no

Attachments:
- [ ] Second opinion
- [ ] Recent UDS

---

Prescriber name…………………………………… Signature……………………………………
Mailing address……………………………………………………………………………………………
Phone (w)………………………………………… Phone (mob)…………………………………
Date ……………………………………………

Subcommittee meetings are scheduled for the second Tuesday of every month, and applications must be received one week prior to the meeting.

Applications should be addressed to: Secretary, PCS, Centre for Drug and Alcohol, NSW Health.
LMB 961 North Sydney, NSW 2059
Fax (02) 9391 9042 Ph: (02) 9391 9244
## Exit from Methadone/Buprenorphine Treatment

*(In accordance with Section 29 of the Poisons and Therapeutic Goods Act 1966)*

**Refer to instructions on the reverse side.**

**Note:** If a client is being transferred from methadone to buprenorphine, or vice versa, with the same prescriber, do not lodge this form.

**Please use block letters.**

<table>
<thead>
<tr>
<th>(P.S.B.) Ref. No.</th>
<th>[Office Use Only]</th>
</tr>
</thead>
</table>

### 1. Surname:

### 2. Given Names:

*(first and middle)*

### 3. Address:

### 4. Suburb: Postcode:

### 5. Gender: M F

### 6. Date of Birth: ____________ / ____________ / ____________

### 7. Is the client EXITING a methadone or buprenorphine program?

- [ ] Methadone  ➔ **Go to Q.9**
- [ ] Buprenorphine

### 8. Was buprenorphine used primarily for withdrawal or maintenance? *(Tick one box only)*

- [ ] Withdrawal
- [ ] Maintenance

### 9. Date of ENTRY to CURRENT program: ____________ / ____________ *(month) (year)*

### 10. Date of LAST DOSE of methadone or buprenorphine dispensed on CURRENT PRESCRIBER’S PRESCRIPTION, including any takeaways: *(see over)*

   ____________ / ____________ / ____________

### 11. LAST DOSE of methadone or buprenorphine: ____________ mg

### 12. Reason for EXITING TREATMENT: *(Tick one box only)*

- [ ] Client did not commence program
- [ ] Program incomplete (mutual agreement)
- [ ] Successfully completed program
- [ ] Ceased to pick up methadone/buprenorphine
- [ ] Treatment terminated involuntarily
  - *Reason for involuntary termination:*

- [ ] Hospitalisation or transfer to other health institution *(not methadone or buprenorphine treatment)*
- [ ] Client deceased
  - *Date of death:____________ / ____________ / ____________ *
  - *Cause of death:*

- [ ] Community transfer within NSW *(from one community prescriber to another)*
  - *Specify new prescriber/clinic:*

- [ ] Transfer from community to gaol prescriber
  - *Specify new gaol community prescriber*

- [ ] Transfer to interstate methadone or buprenorphine program

- [ ] Other, specify:

---

**This client has been discharged from methadone/buprenorphine treatment.**

**Signature (of person discharging client):**

**Date:**

**Prescriber's Name:**

**Address:**

---

New South Wales Opioid Treatment Program
Example of a formal warning letter

It may be advisable to give patients who do not comply with the terms of their treatment agreement (see section 3.12.4 Treatment Agreement on page 24 and section 7.8 Managing difficult behaviour on page 69) a formal written warning that continuing non-compliance will not be tolerated. An example used by the North Coast Health Service is shown below.

North Coast Area Health Service

Day/Month/Year

XXXX

C/- Woodlands Opioid Treatment Clinic

FORMAL WARNING LETTER

It has been brought to our attention that on DAY/MONTH at TIME you verbally abused and threatened two staff in the waiting room of the Woodlands Clinic.

This behaviour will not be tolerated and is in breach of your treatment agreement. You are formally warned that you will be banned from the Clinic if you continue to behave in an aggressive and abusive manner either physically or verbally to staff or other clients.

Furthermore Police will be called and you will be charged for any further offences.

As a consequence of these incidents the following changes will occur as a condition of your continuation on methadone treatment at Woodlands Clinic:

1. Takeaway doses will be suspended immediately.

2. Police will be called and charges laid for any further violent, offensive or criminal conduct such as dealing or diversion of methadone.

3. Failure to adhere to these conditions will lead to withdrawal from methadone and discharge from the Clinic.

4. Your treatment progress and conditions will be reviewed in three months.

[signed]

Director Drug and Alcohol Services                      Chief Executive Officer
Patient identification

Patient identity must be verified before a patient can be admitted to an opioid treatment program.

Group 1
Positive identification may be established by:

- Passport
- Photo license
- Gaol card showing photo, date of birth, MIN number and signature
- Proof of age card

Group 2
Identification may also be established by ANY THREE of the following:

- ATM card
- Bank or credit union statements or passbook
- Birth certificate
- Credit card
- Marriage certificate
- Medicare card
- Pay advice slip
- Paid bills directed to the patient’s current address (eg, gas, telephone, electricity)

Note: Three ATM cards or credit cards are not acceptable.

Group 3
Identification may also be established by ONE item from this group and ONE item from GROUP 2.

- Gaol release slip
- Methadone clinic client ID, as used in transfers between clinics
- Social security or pension card
- License (no photo)

Note: Check that the signature on any document produced as proof of identity matches the signature on the consent section of the application for treatment.
Managing attempted buprenorphine diversion

The following documents are examples of a structured approach to managing attempted diversion of doses, as used in the Buprenorphine Quality Improvement Exercise, Opioid Treatment Program, Western Zone, Sydney South West Area Health Service.

Managing buprenorphine diversion

- All incidents of diversion should be documented on the IIMS record and noted in the medical record.
- The Unit Manager should conduct an interview with the patient involved at the earliest opportunity.
- At this interview the patient is requested to provide an explanation of the events, is reminded of their responsibility to adhere to the rules of the program, and is advised of the implications of further diversion.
- Following this interview and depending on the circumstances surrounding the diversion episode a management plan is devised by treatment team.
- Unit Managers should follow the example set out below when conducting an interview with patients following a diversion episode.

Discuss the event and answer concerns relating to reasons for diverting (eg, dose too high, fear of precipitated withdrawal, being forced to attend by partner, etc). then complete the quality improvement questionnaire — advise that it is confidential.

Summarise the meeting and include this advice:

```
Thanks for coming to meet with me. I assume you are aware staff have identified you as attempting to divert your buprenorphine.

At this interview I would like to get to know little more about the episode and discuss the rules of the program, the implications of repeated diversion and also address concerns you may have about your treatment that may have led to this episode.

After this I would like to ask you some questions about diversion for a project we are conducting. The purpose of the project is to get to know a little more about diversion and how we can address it.

Firstly, I need to be clear with you and state that the unit cannot condone drug diversion regardless of the reason. Staff have very clear obligations to ensure that buprenorphine is taken correctly.

Treatment is voluntary, which means, that if patients do not want to take their buprenorphine they do not have to... if there is a problem with the treatment it can always be managed... So we are often confused why some people attend for dosing but do not take their buprenorphine as expected. Can you tell me what happened?
```

Medication such as buprenorphine can be dangerous if used in ways other than directed or if taken by people not used to taking drugs like it.

As outlined in both our own and the NSW Health treatment agreement diversion is against the rules of the clinic. A second episode of diversion will result in your present buprenorphine treatment being terminated. At this time you may transfer to methadone or undergo a buprenorphine detoxification over a set time (usually 1 week). You may also choose to find another prescriber.

If you have any concerns regarding your treatment please do not hesitate to discuss these with your case manager and prescriber.
## Diversion of buprenorphine assessment form

<table>
<thead>
<tr>
<th>DEMOGRAPHICS</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>MRN</td>
<td>Gender</td>
</tr>
<tr>
<td>Age</td>
<td>Country of Birth</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>REFERRAL DETAILS (please tick)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-referral</td>
<td>Corrections transfer</td>
</tr>
<tr>
<td>Merit</td>
<td>Adult drug court</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TREATMENT DETAILS</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous methadone treatment episodes</td>
<td>0 1 2 3 4+</td>
</tr>
<tr>
<td>Previous buprenorphine episodes</td>
<td>0 1 2 3 4+</td>
</tr>
<tr>
<td>Current buprenorphine dose (enter dose)</td>
<td>milligrams</td>
</tr>
<tr>
<td>Frequency of pick-up</td>
<td>daily</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TREATMENT DETAILS</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of current treatment episode</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TREATMENT DETAILS</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Has anyone explained to you how buprenorphine works and how to take it?</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DIVERSION</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Method of diversion (full details)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DIVERSION</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of times caught diverting dose.</td>
<td>0 1 2 3 4+</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Why did you try to divert? (please tick)</th>
<th>Denies diverting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Denies diverting</td>
<td></td>
</tr>
<tr>
<td>Did not want dose — fear of precipitated withdrawal due to recent opiate use</td>
<td></td>
</tr>
<tr>
<td>Did not want full dose — fear of greater addiction/harder to get off</td>
<td></td>
</tr>
<tr>
<td>Did not want full dose — wanted to detox self</td>
<td></td>
</tr>
<tr>
<td>Did not want full dose — wanted to be able use heroin on top</td>
<td></td>
</tr>
<tr>
<td>Did not want full dose — side effects</td>
<td></td>
</tr>
<tr>
<td>Did not want full dose — I think dose just too high</td>
<td></td>
</tr>
<tr>
<td>Not sure about continuing treatment</td>
<td></td>
</tr>
<tr>
<td>Asked to by a friend</td>
<td></td>
</tr>
<tr>
<td>Heard bad things about this drug</td>
<td></td>
</tr>
<tr>
<td>Other — Specify</td>
<td></td>
</tr>
</tbody>
</table>

---

Clinical guidelines for methadone and buprenorphine treatment of opioid dependence  PAGE 167
If you were successful in taking the buprenorphine outside what did you intend to do with it?

<table>
<thead>
<tr>
<th>Option</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sell it</td>
<td></td>
</tr>
<tr>
<td>Use it later — oral/sublingual — Self</td>
<td></td>
</tr>
<tr>
<td>Use it later — inject — Self</td>
<td></td>
</tr>
<tr>
<td>Use it later — oral/sublingual — other person</td>
<td></td>
</tr>
<tr>
<td>Use it later — inject — other person</td>
<td></td>
</tr>
<tr>
<td>Discard it</td>
<td></td>
</tr>
<tr>
<td>Other — specify</td>
<td></td>
</tr>
</tbody>
</table>

How would you stop diversion of buprenorphine?

BUYING ILLICIT BUPRENORPHINE

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have you ever been offered diverted buprenorphine?</td>
<td>Yes</td>
</tr>
<tr>
<td>Do you know anyone who has been offered diverted buprenorphine?</td>
<td>Yes</td>
</tr>
<tr>
<td>Have you ever bought diverted buprenorphine?</td>
<td>Yes</td>
</tr>
<tr>
<td>Do you know anyone who has bought diverted buprenorphine?</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Overall how easy would it be for you to get buprenorphine on the streets?

<table>
<thead>
<tr>
<th>Difficulty Level</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Very easy</td>
<td></td>
</tr>
<tr>
<td>easy</td>
<td></td>
</tr>
<tr>
<td>possible</td>
<td></td>
</tr>
<tr>
<td>difficult</td>
<td></td>
</tr>
<tr>
<td>very difficult</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>What is the cost of an 8 mg buprenorphine tablet?</td>
<td>$ ______ or NA</td>
</tr>
<tr>
<td>What is the cost of a 2 mg buprenorphine tablet?</td>
<td>$ ______ or NA</td>
</tr>
</tbody>
</table>

For what reasons do you think most people buy diverted buprenorphine (eg, to help detox, to have in an emergency if they run out of heroin, get stoned, other)?

Other comments:
Drugs of addiction (Schedule 8 of the NSW Poisons List)

Not all Schedule 8 substances are listed here since many are not currently available for use in Australia. Some brand names have been inserted alphabetically in capital letters. Veterinary lines are indicated thus: (Vet.). Salts, derivatives, preparations and admixtures of the substances listed are controlled in the same way as the substances themselves.

<table>
<thead>
<tr>
<th>Substance</th>
<th>Substance</th>
<th>Substance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alfentanil</td>
<td>Flunitrazepam</td>
<td>OXYNORM</td>
</tr>
<tr>
<td>Amphetamine (1)</td>
<td>FORTRAL</td>
<td>PALFIUM</td>
</tr>
<tr>
<td>Amylobarbitone (6)</td>
<td>Hydrocodone</td>
<td>Papaveretum</td>
</tr>
<tr>
<td>ANAMORPH</td>
<td>Hydromorphone</td>
<td>Pentazocine</td>
</tr>
<tr>
<td>ATTENTA (1)</td>
<td>HYPNODORM</td>
<td>Pentobarbital (6)</td>
</tr>
<tr>
<td>BIDONE FORTE</td>
<td>IMMOBILON (Vet. Etorphine)</td>
<td>Pethidine — <em>all forms</em> (inc. Vet)</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>KAPANOL</td>
<td>Phendimetrazine (1)</td>
</tr>
<tr>
<td>Butobarbital</td>
<td>Kaolin and Opium Mixture</td>
<td>Phenmetrazine (1)</td>
</tr>
<tr>
<td>Butorphanol</td>
<td>LEPTAN (Vet. Fentanyl)</td>
<td>Phenoperidine</td>
</tr>
<tr>
<td>Camphorated opium tincture</td>
<td>Methadone</td>
<td>Pholcodine (5)</td>
</tr>
<tr>
<td>Cocaine — <em>all forms</em></td>
<td>METHONE (Vet. Methadone)</td>
<td>Quinalbarbital</td>
</tr>
<tr>
<td>Codeine (2)</td>
<td>Methylamphetamine (1)</td>
<td>RAPIFEN</td>
</tr>
<tr>
<td>Cyclobarbital</td>
<td>Methylphenidate (1)</td>
<td>Remifentanil</td>
</tr>
<tr>
<td>Dexamphetamine (1)</td>
<td>MORPHALGIN</td>
<td>RITALIN</td>
</tr>
<tr>
<td>Dextromoramide</td>
<td>Morphine — <em>all forms</em></td>
<td>ROHYPNOL</td>
</tr>
<tr>
<td>Dextropropoxyphene (3)</td>
<td>MS CONTIN</td>
<td>Secbutobarbitone</td>
</tr>
<tr>
<td>Diethylthiambutene</td>
<td>MS MONO</td>
<td>SUBLIMAZE</td>
</tr>
<tr>
<td>Dihydrocodeine</td>
<td>NEURAMYL</td>
<td>Subutex</td>
</tr>
<tr>
<td>DILAUID</td>
<td>Normethadone</td>
<td>Sufentanil</td>
</tr>
<tr>
<td>DOLOREX (Vet. Butorphanol)</td>
<td>OPERIDINE</td>
<td>TEMGESIC</td>
</tr>
<tr>
<td>DUROGESIC</td>
<td>Opium — <em>all forms</em></td>
<td>TORBUGESIC (Vet. Butorphanol)</td>
</tr>
<tr>
<td>ENDONE</td>
<td>ORDINE</td>
<td>ULTIMA</td>
</tr>
<tr>
<td>Ethylmorphine (4)</td>
<td>Oxycodone</td>
<td></td>
</tr>
<tr>
<td>Etorphine</td>
<td>OXYCONTIN</td>
<td></td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Oxymorphone</td>
<td></td>
</tr>
</tbody>
</table>

(1) Indicates an amphetamine or amphetamine-like substance subject to the provisions of Clause 121, *Poisons and Therapeutic Goods Regulation 2002*. These substances may not be prescribed by dentists or veterinary surgeons.

Medical practitioners may prescribe these substances for therapeutic use if authorised generally or in a particular case to do so by the Department of Health.

(2) Codeine is exempted from Schedule 8:
   (a) in compounded divided preparations containing 30 mg or less of codeine per dosage unit;
   (b) in other compounded preparations containing 1.0% or less of codeine.

(3) Dextropropoxyphene is exempted from Schedule 8:
   (a) in divided preparations containing 135 mg of dextropropoxyphene or less per dosage unit;
   (b) in liquid preparations containing 2.5% or less of dextropropoxyphene.

(4) Indicates a substance that is exempted from Schedule 8:
   (a) in compounded divided preparations containing 100 mg or less of that substance per dosage unit;
   (b) in other compounded preparations containing 2.5% or less of that substance.

(5)Pholcodine is exempted from Schedule 8:
   (a) in divided preparations containing 100 mg or less of pholcodine per dosage unit;
   (b) in undivided preparations containing 2.5% or less of pholcodine.

(6) Amylobarbitone and pentobarbital are exempted from Schedule 8 when packed and labelled for injection.

“Compounded” in relation to a substance means combined with one or more other therapeutically active substances in such a way that it cannot be separated from them by simple dissolution or by other simple physical means.

For copies of this guide or further information, contact the Duty Pharmaceutical Adviser, Pharmaceutical Services Branch, on (02) 9879 3214.
Patient consent form for buprenorphine treatment during pregnancy or breastfeeding

The following consent form and letter to a referring general practitioner are examples from documents developed by the Turning Point Alcohol and Drug Centre and The Royal Women’s Hospital, Melbourne.

I, ………………………………………….. am currently in treatment with buprenorphine for the management of my opioid dependence, and wish to continue treatment with buprenorphine during my pregnancy/period of breastfeeding, rather than:

- transfer to methadone, or
- withdraw from buprenorphine

In making this decision, I understand that:

- the safety of buprenorphine during pregnancy or breastfeeding remains uncertain at this stage
- pregnancy and breastfeeding are currently listed as contraindications for the use of buprenorphine in Australia by the Therapeutic Goods Administration
- I will need to attend regularly (and as directed) for antenatal care at …………………………………………..………… Hospital
- I will need to attend regularly for appointments with my treatment team at …………………………………………………………………………..

Name: …………………………………………….
Signed: ………………………………………... Date …… / ….. / ………..
Witness: ………………………………………... Date …… / ….. / ………..

Letter from obstetric service to general practitioners managing pregnant women on buprenorphine

Dear Dr ………..,

Thank you for referral of Ms…………………………..for management of her pregnancy.

As you are aware, Ms……………………..is opioid dependent and currently being maintained on buprenorphine as an opioid substitution agent. Buprenorphine is listed as a category C medication in pregnancy by the Australian Drug Evaluation Committee. The Therapeutic Goods Administration of Australia has listed pregnancy and breastfeeding as contraindications for the use of buprenorphine.

I have recommended that Ms ……………………. transfers to methadone for the duration of her pregnancy. However, she has decided, after being aware of the lack of adequate data on the safety of buprenorphine in pregnancy, to continue on buprenorphine rather than transfer to methadone.

I am happy to continue to manage her obstetric care.

Yours sincerely,

…………………….
Neonatal withdrawal scoring chart

The following chart is an amended version of the original by L Finnegan, and has been reproduced with the permission of the Royal Prince Alfred Hospital.

For information about how to use this chart and monitor and treat neonatal withdrawal, contact your local drug and alcohol medical specialist or the specialist Drug and Alcohol Advisory Service on 1800 023 687.

Royal Prince Alfred Hospital modified Finnegan Neonatal Abstinence Scoring System

<table>
<thead>
<tr>
<th>System</th>
<th>Score</th>
<th>Date, Time (hrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Central nervous system disturbances</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High pitched cry</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Continuous high pitched cry</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Sleeps &lt;1 hour after feeding</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Sleeps &lt;2 hours after feeding</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Sleeps &lt;3 hours after feeding</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Mild tremors, disturbed</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Mod-severe tremors, disturbed</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Mild tremors, undisturbed</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Mod-severe tremors, undisturbed</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Increased muscle tone</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Excoriation (specify area)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Myoclonic jerks</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Generalised convulsions</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td><strong>Metabolic/vasomotor/respiratory/disturbances</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever (37.3–38.3˚C)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Fever (38.4˚C and higher)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Frequent yawning (3–4 times)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Nasal stuffiness</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Sneezing (&gt;3–4 times)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Nasal flaring</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Respiratory rate &gt;60/min</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Respiratory rate &gt;60/min with retractions</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td><strong>Gastrointestinal disturbances</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excessive sucking</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Poor feeding</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Regurgitation</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Projectile vomiting</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Loose stools</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Watery stools</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL SCORE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SCORER’S INITIALS</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Lipsitz score for neonatal abstinence syndrome

<table>
<thead>
<tr>
<th>Signs</th>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tremors</td>
<td>0</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Minimally increased when hungry or disturbed</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Moderate or marked increase, subside when fed or held snuggly</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Marked increase or continuous even when undisturbed, going on to seizure like movements</td>
</tr>
<tr>
<td>Irritability (excessive crying)</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Slightly increased</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Moderate to severe when disturbed or hungry</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Marked even when undisturbed</td>
</tr>
<tr>
<td>Reflexes</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>Increased</td>
<td>Marked increase</td>
</tr>
<tr>
<td>Stools</td>
<td>Normal</td>
<td>Explosive but normal frequency</td>
</tr>
<tr>
<td></td>
<td>Explosive, more than 8 per day</td>
<td></td>
</tr>
<tr>
<td>Muscle tone</td>
<td>Normal</td>
<td>Increased</td>
</tr>
<tr>
<td></td>
<td>Rigidity</td>
<td></td>
</tr>
<tr>
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<td>Redness of knees or elbows</td>
</tr>
<tr>
<td></td>
<td>Breaking of skin</td>
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<tr>
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</tr>
<tr>
<td>Vomiting</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Fever</td>
<td>No</td>
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</table>
It is sometimes necessary to discharge a patient from treatment for the safety or wellbeing of the patient, other patients or staff. At the beginning of methadone or buprenorphine treatment, patients should be provided in writing with the conditions under which they may be involuntarily discharged. All patients should have access to procedures intended to resolve conflicts between themselves and those responsible for their care.

If staff have determined that a patient has breached the conditions of the treatment service, that patient may be discharged involuntarily. The following will then take place:

- the patient is informed of the breach by the end of the next weekday
- a meeting is arranged with the patient to negotiate the consequence of the breach within 48 hours of the patient being notified
- the patient is informed of the appeals mechanism at the time of the initial meeting
- the event and the resultant action is documented in the patient record
- if a patient is discharged from the program and feels the decision to be contrary to the contract, the patient has the right of appeal.

**Process for appeals**

**Patients** will:

- make verbal requests for appeal within three days of being informed of the team decision
- put the appeal in writing within 24 hours of making the verbal request
- present information to the appeal panel on the reasons for the appeal.

The MACS information line (1800 642 4280) and NUAA (1800 644 413) are available to assist with appeals.

**Pharmacotherapies staff** will:

- inform the patient of the appeals process
- discuss the appeal with the prescriber and the relevant staff before the appeals hearing
- organise an appeal panel within 48 hours of the written request for an appeal being received
- present information to the appeal panel on the background to the decision which led to the appeal.

If required a member of staff will help the patient with the appeal process on request, including attending the appeal. This is not to be seen as support of the appeal. It is also possible to have an outside person attend as a support person. In the case of appeals, dosing times may be altered if safety at the clinic is considered to be at risk. Discussion of the recommendations will be put to the team for final approval. Final recommendations will be made in writing to the patient. The outcome of the appeal process is final.

**Appeal panel**:

- hears both sides of the appeal from the patient and the staff
- makes a decision on the information presented and in line with the pharmacotherapy services rules and regulations
- reports the results of the decision to the staff for approval
- reports recommendations of the final decisions in writing to the patient
- documents the appeal process and decision in the patient record

**Outcome**:

A patient has the right of appeal when involuntarily discharged from a pharmacotherapy service. All patients should have a fair opportunity to present their case. If possible, patients should be retained in the current treatment program pending the resolution of the complaint.
Acknowledgements

The Quality In Treatment Advisory Group developed this document for the Mental Health and Drug & Alcohol Office of the NSW Department of Health. It makes frequent use of two documents produced by the Australian Government Department of Health and Ageing:


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Mr D Reilly
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Dr Adam Winstock

Editorial assistance: Craig Bingham (Australasian Medical Publishing Company)
Guidelines regarding the use of Suboxone® Sublingual Film in the management of opioid dependence

What is Suboxone® Sublingual Film?
Suboxone® Sublingual Film is a new formulation of Suboxone licensed for the treatment of opioid dependence, with the same active ingredients and doses as the sublingual tablets (buprenorphine and naloxone in 2/0.5mg and 8/2mg preparations). The Films have a lime flavour and are orange in colour with the strength printed in white (N2 or N8). Each Film is individually packaged in child resistant sachets.

Rationale for Use
Suboxone Film makes supervised dosing easier and reduces the time required for effective supervision. Whereas Suboxone tablets require 3 to 10 minutes to dissolve, the Film adheres within seconds to the oral mucosa and is difficult to remove after 30 to 60 seconds. This should reduce the potential for diversion and misuse of the medication.

How does Suboxone Film compare to tablets?
– Plasma concentrations: Suboxone Film and tablets deliver similar plasma concentrations of buprenorphine, the active medication in Suboxone tablets. Maximum blood concentrations (Cmax) appear to be higher for the Film than the tablets, but the total amount released over a 24-hr period is comparable, and any differences are unlikely to be clinically significant.

– Effectiveness: In an Australian multisite, double-blind randomised controlled trial, in which patients were treated with either Suboxone Film or tablets, there were no significant differences in patient ratings of sedation, intoxication, or withdrawal symptoms over a 24 hour period, or in measures of other drug use, psychosocial function or quality of life between the two groups.
– **Side effects**: The frequency, severity and range of side effects to the Film appear to be broadly the same as for the tablets.

**Transferring from tablet to Film**

The change from Suboxone tablets to Film should be based on a discussion between the patient and their prescriber prior to any transfer. The prescriber should provide an opportunity for the patient to ask questions, provide written information, and obtain informed consent. Important points to address include:

1. What is Suboxone Film, and how is it taken sublingually?
2. Potential advantages and disadvantages of the Film, including:
   – A quicker dosing time (30-60 sec) is possible with the Film, improving convenience for both the patient and dosing staff.
   – The Film has a lime flavour that is rated more favourably than the tablets by many patients.
   – The packaging of the Film is more tamper-proof and child-resistant than Suboxone tablets.
3. The Film and tablets are generally equivalent in dose, and most patients will not require a dose adjustment when changing between tablets and Film. However, some patients may experience a greater (or lesser) effect from the Film, and a minor dose adjustment may be warranted after review with their prescriber. Patients should be cautioned against driving or operating heavy machinery until they are accustomed to the effect of the Film.

The change from tablets to Film should be discussed with the patient’s dosing site (pharmacy or clinic) prior to transfer to ensure they are able to provide the Film formulation.

**How to prescribe**

– NSW Health Department authority procedures remain the same as for Suboxone tablets. No change is required if an authority is already in place for Suboxone tablets.

– The use of the Film must be specified on the prescription (e.g. Suboxone Film 16mg SL daily). The same formulation should be prescribed for both supervised and unsupervised doses - do not prescribe the Film for supervised dosing and tablets for take-aways.

– Prescriptions can only be written for combinations of the available unit doses (2mg/0.5mg and 8mg/2mg), as pharmacists cannot dispense partial doses (i.e. they cannot accurately break or cut Film). Patients on doses lower than 2mg will need to use Subutex 0.4mg SL tablets.

– Patients should be transferred directly over to the same dose of Film as they are currently receiving in tablet form. For example, a patient on 16mg daily of tablets should change directly over to 16mg daily of Film, with no need for re-induction. Some patients may warrant a dose adjustment after transfer, and a review of the patient soon after changing to the Film is recommended.

– All prescribing practices for Suboxone Film remain the same as for the tablet, including induction and stabilisation procedures, maintenance doses, maximum doses, and access to take-away or unsupervised doses.

– Suboxone Film can be misused in a manner similar to other pharmaceutical opioids. Clinical monitoring appropriate to the patient’s level of stability is essential.
How to dose

Preparation & presentation (see Figures)

1. Collect and check the total dose of unopened sachets against the prescription. Suboxone Film should not be cut by the nurse or pharmacist (e.g. half a 2/0.5 mg Film in order to achieve a 1mg dose). Dosing staff should clarify such prescriptions with the prescriber.

2. Fold the sachet along the dotted line and tear down at the slit as indicated on the packaging.

3. Present all Films to the patient at once in the opened sachets or in an appropriate container (such as a transparent 20ml plastic medication cup) rather than one by one, as this increases the risk of dosing errors and interferes with supervision. The nurse or pharmacist must avoid handling the Film with bare fingers and use tweezers if necessary to remove the Film from the packaging. If it is necessary for the nurse or pharmacist to touch the Film with their fingers, then a disposable glove should be used.

4. If the Film is accidently dropped, or becomes wet before being given to the patient it is to be destroyed and a new dose dispensed. Follow the requirements under Poisons and Therapeutic Goods Regulation 2008 in relation to the procedures for the loss, and destruction, of Schedule 8 drugs.

5. Under normal circumstances no significant active drug will remain on the inside of the packaging, and empty sachets should be disposed of discretely in normal rubbish containers.

Figure 1

Figure 2

Figure 3

Figure 4

Diagrams of patient removing the Film for administration
Administration and Supervision
As with sublingual tablets, patients should avoid eating immediately prior to dosing with the Film to ensure the mouth is free of material that may interfere with absorption of the medication. The patient should have a sip of water to moisten the mouth prior to dosing.

1. Instruct the patient to make sure their hands are clean (e.g. wash hands or use hand sanitiser) and ensure hands are completely dry before handling the Film.
2. The patient should hold the Film between two fingers by the outside edge of the Film (Figure 5) and should place each Film individually sublingually (under the tongue) close to the base on either side (Figure 6). Films should not overlap, and if more area is required (e.g. the dose requires more than two Films) placement can be buccal (against the oral mucosa on the inside of the cheek). Although buccal dosing is not recommended by the manufacturer, evidence suggests comparable bioavailability between sublingual and buccal administration.
3. Some patients may report accidently placing the Film against their teeth or tongue. Experience to date indicates this has little impact upon the clinical effects of the Film.

4. Supervision: adherence of the Film occurs within seconds, and the Film is difficult to dislodge or remove after 30 to 60 seconds. The patient need only remain under supervision for 30 seconds if on low doses (<16mg) or 1 minute if on high doses (> 16mg). Adherence to the mucosa can be delayed if Films are placed overlapping, and longer supervision time may be required. The nurse or pharmacist must ensure that appropriate procedures are in place, including monitoring the time elapsed after administration, to minimise the risk of diversion.
5. The Film takes approximately 2 to 5 minutes to dissolve and be absorbed. The patient should not chew, swallow or talk for several minutes as this may interfere with absorption. As with other sublingual medication, doses do not need to be replaced if the patient vomits after this time.

Which formulation?
If there is confusion regarding the formulation to be dispensed (e.g. the prescription is unclear), clarification should be sought by the nurse or pharmacist from the prescriber prior to dosing if possible. If clarification is unable to be obtained, the patient should be dosed with the available Suboxone formulation at the specified dose and the prescriber notified at the next possible opportunity. Where both formulations are available, the pharmacist or nurse should administer the usual formulation as identified on previous prescriptions and by the patient’s report.
Where the prescription is for a formulation that is not available at the pharmacy or clinic, the pharmacist or nurse should seek clarification from the prescriber prior to dosing if possible. If clarification is unable to be obtained, the patient should be dosed with the available formulation of Suboxone at the specified dose until the prescriber can be contacted at the next possible opportunity.

**Recording as a Schedule 8 medication**
Pharmacists and nurses must record the dispensing and administration of this medication in accordance with the requirements of the Poisons and Therapeutic Goods Regulation 2008, with drug register entries which include the details of the receipt, supply (administering/dispensing), and balance on hand, and with each strength in separate sections. Suboxone Film must also be stored in the drug safe when not in immediate use.

**Safety issues**
- Suboxone Film is designed as a sublingual formulation. Use by any other use route (including injecting or snorting) is not recommended. Injecting can be associated with damage to injecting sites and infections.
- Buprenorphine is an opioid medication and can result in sedation, reduced respiration, overdose and death if taken by a person not prescribed the medication (e.g. a child), or if mixed with alcohol or other sedative drugs. Contact the NSW Poisons Information Centre on 13 11 26 or call an ambulance if there are any concerns.
- **Pregnancy:** As with Suboxone tablets, Suboxone Film is not recommended in pregnancy due to the uncertain safety of naloxone in pregnancy. Pregnant or breastfeeding patients should commence (or be transferred) to Subutex (buprenorphine mono) tablets instead of Suboxone products.

**Storage**
- After dispensing, the Film must be stored safely, in its original packaging, away from children or other persons who may accidently take the medication or deliberately misuse it.
- The packaging should only be opened when the dose is to be used. It should not be left unattended, especially in the presence of children.
- The Film must be stored below 25°C. Patients should not store the Film on their person (e.g. in their pocket) or in hot areas (e.g. in the glove box of a car in the sun) for long periods of time, as it may be damaged.

This document reflects what is currently regarded as safe practice, however, as in any clinical situation there may be factors which cannot be covered by a single set of guidelines, this document does not replace the need for the application of clinical judgment to each individual presentation.

Whilst the Information contained in these guidelines has been compiled with all due care, NSW Health does not warrant or represent that the Information is free from errors or omission. Further, changes in circumstances after the time of publication may impact on the accuracy of the information.
Information for staff dispensing or administering Suboxone® Sublingual Film

What is Suboxone® Sublingual Film?
Suboxone® Sublingual Film is a new formulation of Suboxone with the same active ingredients and doses as the sublingual tablets (buprenorphine and naloxone in 2/0.5mg and 8/2mg preparations)\(^1\). They are packaged in individual sachets in boxes of 28. The Films are orange in colour with the strength printed in white (N2 or N8), and have a lime flavour, often preferred to the lemon-lime flavour of tablets.

![Suboxone® Sublingual Film](image)

Actual size of each Film: 2.2cm x 1.3cm

Suboxone Film will make supervised dosing easier by reducing the time required for effective supervision. Whereas Suboxone tablets require 3 to 10 minutes to dissolve, the Film adheres within seconds to the oral mucosa and is difficult to remove after 30 to 60 seconds. Bioavailability studies suggest that the Film and tablets produce similar plasma levels. Maximum blood concentration may be slightly higher for the Film but total plasma levels over 24 hours are comparable. In Australian studies, there were no significant differences in the dose effects or side effects of the Film and tablets. Although dose adjustment should not usually be needed when transferring from tablet to Film, some patients require re-assurance, and the prescriber may consider a dose adjustment after review.

Supervised dosing procedure
1. **Prior to dosing**: Advise the patient not to eat immediately before dosing, as it may interfere with absorption. Offer a sip of water to moisten the mouth. Ensure the patient’s hands are clean and dry as the Film may stick to wet hands and make it difficult to place them correctly in the mouth.
2. **Collect the Films** needed to make up the dose and check against the prescription. Films should not be cut-up to manipulate dose (e.g. half a 2/0.5mg Film to achieve a 1/0.25mg dose). Clarify with the prescriber in such an event.
3. **Open all packages** (bend along dotted line and tear at perforation) and offer the open packages to the patient, who removes the Films from the packages one at a time to place in their mouth, OR - remove all Films from packages and place into an appropriate container (e.g. 20ml transparent plastic medication bottle).

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\(^1\) Suboxone Film also contains acesulfame potassium, citric acid anhydrous, maltitol solution, hypromellose, polyethylene oxide, sodium citrate anhydrous, lime flavour, Sunset Yellow FCF and a white printing ink.
cup) and offer to the patient to place in their mouth one at a time. The nurse or pharmacist must avoid handling the Film with their bare fingers and use tweezers if necessary to remove the Film from the packaging. If it is necessary for the nurse or pharmacist to touch the Film with their fingers, then a disposable glove should be used.

4. **Observe correct placement of Films.** Patients should hold the Film by its edges, and place sublingually one at a time. If multiple Films are needed, the first two are placed under the tongue either side of the frenulum. Films should not overlap, and if more area is required (e.g. the dose requires more than two Films) placement can be buccal (against the oral mucosa on the inside of the cheek). Although buccal dosing is not recommended by the manufacturer, evidence suggests comparable bioavailability between sublingual and buccal administration.

5. Advise the patient not to attempt to move the Films once they have been placed in the mouth, nor to chew or swallow the Films until they have fully dissolved (generally 2 to 5 minutes). If Films accidentally stick on top of the tongue or to the teeth, reassure the patient that buprenorphine will still be absorbed and to keep the mouth closed with mucous membranes in contact with the Films as they dissolve.

6. **Supervision time:** Films adhere to mucous membranes within seconds and are difficult to remove within 30-60 seconds, so under normal circumstances, post-dose supervision does not need to exceed one minute. Discourage the patient from overlapping Films when placing in the mouth, as this impairs adherence to the mucosa, and prolongs the time required for supervision. The nurse or pharmacist must ensure that appropriate procedures are in place, including monitoring the time elapsed after administration, to minimise the risk of diversion.

**Recording, storing and disposal of Film and packaging**
- Suboxone Film is a Schedule 8 preparation and must be stored in the drug safe except when in immediate use.
- Records of the dispensing and administration of this medication must in accordance with the requirements of the Poisons and Therapeutic Goods Regulation 2008, with drug register entries which include the details of the receipt, supply (administering/dispensing), and balance on hand, and with each strength in separate sections.
- If the Film is accidently dropped, or becomes wet before being given to the patient it is to be destroyed and a new dose dispensed. Follow the requirements under Poisons and Therapeutic Goods Regulation 2008 in relation to the procedures for the loss, and destruction, of Schedule 8 drugs.
- No active drugs will remain on the inside of the packaging under normal circumstances, and empty sachets should be discarded discreetly in the normal rubbish.

**Advice for patients with ‘take-away’ (unsupervised) Film**
- Store Films in a secure, cool place below 25°C. For example, do not leave in a car’s glove box on a hot day.
- Do not remove the Film from the packaging until you are ready to use them. The appearance of the Film may be attractive to children.

If the prescriber specifies a form of Suboxone that is not immediately available (e.g. Film but you only stock tablets), contact the prescriber regarding appropriate action. If it is not possible to contact them, administer the available form until contact can be made.
Information for prescribers of Suboxone® Sublingual Film

What is Suboxone® Sublingual Film?
Suboxone® Sublingual Film is a new formulation of Suboxone with the same active ingredients and doses as the tablets (buprenorphine and naloxone in 2/0.5mg and 8/2mg preparations). The Films have a lime flavour and are orange in colour with the strength printed in white (N2 or N8). Suboxone Film makes supervised dosing easier and reduces the time required for effective supervision. Whereas Suboxone tablets require 3 to 10 minutes to dissolve, the Film adheres within seconds to the oral mucosa and is difficult to remove after 30 to 60 seconds. This should reduce the potential for diversion and misuse of the medication. Bioavailability studies suggest that the Film and tablets produce similar plasma levels. Although peak plasma concentrations are slightly higher for the Film, total ‘area under the curve’ is comparable. Australian studies indicate no significant differences in the dose effects, side effects or clinical outcomes for the Film and tablets.

Transferring from tablet to Film
Discuss changing from Suboxone tablets to Film with the patient prior to any transfer. Provide an opportunity for questions, provide written information, and obtain informed consent. Important points to address include what is Suboxone Film, how is it taken sublingually, and potential advantages and disadvantages of the Film, including:

- A quicker supervised dosing time with the Film (30-60 seconds), improving convenience for both the patient and dosing staff.
- The Film has a lime flavour, rated more favourably than the tablets by many patients.
- Each Film is individually packaged in sachets that are more child-resistant than Suboxone tablets.

Patients should be transferred directly over to the same dose of Film as they currently receive in tablet form without the need for re-induction. Reassure patients that the Film and tablets are generally equivalent in dose, and most patients do not require a dose adjustment, although some may warrant a minor dose change after review. The change from tablets to Film should be discussed with the patient’s dosing site (pharmacy or clinic) prior to transfer to ensure they are able to provide the Film formulation.
How to prescribe

- NSW Health Department authority procedures remain the same as for Suboxone tablets. No change is required for patients already with an authority for Suboxone tablets.
- The use of the Film must be specified on the prescription (e.g. Suboxone Film 16mg SL daily). The same formulation is to be prescribed for both supervised and unsupervised doses.
- Prescriptions can only be written for combinations of the available unit doses (2mg/0.5mg and 8mg/2mg), as pharmacists cannot dispense partial doses (i.e. they cannot accurately break or cut Film). Patients on doses lower than 2mg will need to use Subutex 0.4mg SL tablets.
- All prescribing practices for Suboxone Film remain the same as for the tablet, including induction and stabilisation procedures, maintenance doses, maximum doses, and access to take-away or unsupervised doses.
- Suboxone Film can be misused in a manner similar to other pharmaceutical opioids. Clinical monitoring appropriate to the patient’s level of stability is essential.
- Pregnancy: As with Suboxone tablets, Suboxone Film is not recommended in pregnancy due to the uncertain safety of naloxone in pregnancy. Pregnant or breastfeeding patients should commence (or be transferred) to buprenorphine-mono tablets instead of Suboxone products.

Dosing technique

1. Patient should not eat for several minutes before or after dosing, as this can interfere with absorption.
2. Patients should hold the Film by its edges, and place each Film one at a time sublingually. If multiple Films are used, the first two are placed sublingually either side of the frenulum. Films should not overlap, and if more area is required (e.g. the dose requires more than two Films) placement can be buccal (against the oral mucosa on the inside of the cheek). Although buccal dosing is not recommended by the manufacturer, evidence suggests comparable bioavailability between sublingual and buccal administration.
3. Films adhere to mucous membranes within seconds and are difficult to remove after 30-60 seconds, so under normal circumstances, post-dose supervision does not need to exceed one minute.

Advice for patients with ‘take-away’ (unsupervised) Film.
Suboxone Films should be stored in a secure, cool place below 25°C. For example, do not leave in a car’s glove box on a hot day. Do not to remove Films from the sachet until you are ready to use them, as the appearance of the Films may be attractive to children.
How do I change from Subutex or Suboxone Tablets to Suboxone Film?

Talk to your treatment providers about the decision to change to the Film. Differences between tablets and Film are:
- less time needed for supervising Suboxone Film (usually less than 1 minute) compared to tablets (usually 3 to 10 minutes)
- the Film is lime flavoured, instead of the lemon-lime of the tablets.
- the Film is individually wrapped in more child-resistant packaging.

Most people do not experience any difference between the dose effects or side effects of Suboxone Film and tablets. However, everybody is different, and some people may need a small dose increase or decrease after changing between tablets and Film – talk to your treatment provider if you have any concerns.

Safety Issues

Suboxone Film is only meant to be taken in your mouth (under the tongue or against the cheek), and should not be taken in other ways (swallowed, injected, snorted). Injecting Suboxone can cause infections and damage to injecting sites.

Suboxone Film contains buprenorphine, an opioid medication that can cause drowsiness, slowed breathing, overdose and death if taken by anyone other than who it’s prescribed for (e.g. a child), and/or if it is mixed with alcohol or other sedating medications or drugs. Please contact the NSW Poisons Information Centre on 13 11 26 or call an ambulance if there are any concerns.

Storage

Store Suboxone Film in a cool (below 25 degrees Celsius) and dry place that is out of reach of children or others. DO NOT store Suboxone Film in hot areas for a long time (e.g. in the glove box of a car).

Useful Contact Details

For more information contact your treatment providers, and/or
NSW Poisons Information Centre: 13 11 26
Methadone Advice and Conciliation Service (MACS): 1800 642 428
How is Suboxone Film taken?

Suboxone Film is taken sublingually (under your tongue) much like Suboxone tablets. The Film sticks to the lining of your mouth, so this shows it difficult to place the Film correctly. Hold the Film by its edges (Figure 2), if you take more than one Film and place it under your tongue (Figure 2). If you have more than one Film and place it under your tongue (Figure 2). It will still stick to your teeth or tongue. If there is not enough room under your tongue, the Film will still stick to the lining of your mouth, as this may reduce the absorption and effects of the buprenorphine.

Wash and dry your hands before handling the Film (wet fingers can make the Film stick to your teeth or tongue). If you have more than one Film and place it under your tongue (Figure 2), it will still stick to the lining of your mouth, as this may reduce the absorption and effects of the buprenorphine. Empty wrappings in the normal rubbish after dosing. Wash and dry your hands before handling the Film (wet fingers can make the Film stick to your teeth or tongue). If you prevent sticking of the Film, aspirate any remaining material into the mouth or larynx. Empty wrappings in the normal rubbish after dosing. Wash and dry your hands before handling the Film (wet fingers can make the Film stick to your teeth or tongue). If you prevent sticking of the Film, aspirate any remaining material into the mouth or larynx.

Figure 1

Diagrams of patient administering the Film

Figure 2

How is Suboxone Film taken?

Wash and dry your hands before handling the Film (wet fingers can make the Film stick to your teeth or tongue). If you have more than one Film and place it under your tongue (Figure 2), it will still stick to the lining of your mouth, as this may reduce the absorption and effects of the buprenorphine. Empty wrappings in the normal rubbish after dosing. Wash and dry your hands before handling the Film (wet fingers can make the Film stick to your teeth or tongue). If you prevent sticking of the Film, aspirate any remaining material into the mouth or larynx. Empty wrappings in the normal rubbish after dosing. Wash and dry your hands before handling the Film (wet fingers can make the Film stick to your teeth or tongue). If you prevent sticking of the Film, aspirate any remaining material into the mouth or larynx.

Figure 3

Diagrams of patient removing the Film for administration

Figure 4

Figure 5

Figure 6

Diagrams of patient removing the Film for administration

Page 3