Public Assessment Report

Paracetamol 500mg Soluble Tablets

PL 16363/0127
PL 16363/0194
# PARACETAMOL 500MG SOLUBLE TABLETS

**PL 16363/0127**  
**PL 16363/0194**  
**UKPAR**

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PARACETAMOL 500MG SOLUBLE TABLETS

PL 16363/0127
PL 16363/0194

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) has granted Milpharm Limited Marketing Authorisations (licences) for the medicinal product Paracetamol 500mg Soluble Tablets (PLs 16363/0127, 0194). PL 16363/0127 is a general sale list [GSL] medicine while PL 16363/0194 is a pharmacy [P] medicine. Paracetamol 500mg Soluble Tablets is used for the relief of painful and feverish conditions.

The active ingredient paracetamol is a pain-killer which also acts to bring down the body temperature in case of fever.

The clinical data presented to the MHRA, before licensing, demonstrated that Paracetamol 500mg Soluble Tablets is essentially similar or equivalent to the approved product, Panadol Soluble Tablets 500mg, and as such can be used interchangeably.

No new or unexpected safety concerns arose from these applications and it was decided that the benefits of using Paracetamol 500mg Soluble Tablets outweigh the risks, hence Marketing Authorisations have been granted.
PARACETAMOL 500MG SOLUBLE TABLETS
PL 16363/0127
PL 16363/0194

SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy the UK granted marketing authorisations for the medicinal product Paracetamol 500mg Soluble Tablets (PLs 16363/0127, 0194) to Milpharm Limited on 23 May 2006. PL 16363/0127 is a general sale list medicine while PL 16363/0194 is a pharmacy medicine.

The applications were submitted as abridged applications according to Article 10.1(a)(iii) of Directive 2001/83/EC, claiming essential similarity to Panadol Soluble 500mg Tablets, which was authorised in the UK on 12 January 1982.

Paracetamol 500mg Soluble Tablets contain the active ingredient paracetamol and is recommended for the treatment of most painful and febrile conditions, for example, headache including migraine and tension headaches, toothache, neuralgia, backache, rheumatic and muscle pains, dysmenorrhoea, sore throat and for relieving the fever, aches and pains of colds and flu.

Paracetamol has analgesic and antipyretic effects similar to those of aspirin and is useful in the treatment of mild to moderate pain. It has weak anti-inflammatory effects.
PHARMACEUTICAL ASSESSMENT

LICENCE No.: PL 16363/0127, 0194
PROPRIETARY NAME: Paracetamol 500mg Soluble Tablets
ACTIVE(S): Paracetamol Ph.Eur.
COMPANY NAME: Milpharm Limited
EC ARTICLE: 10.1 (a)(iii)
LEGAL STATUS: GSL, P

REQUESTS FOR INSPECTION ACTION PRIOR TO AUTHORISATION

No inspection request prior to authorisation as a copy of the manufacturing licence is provided for the named manufacturing site.

INTRODUCTION

These are standard national abridged Marketing Authorisation Application containing 500mg paracetamol as the active ingredient in a soluble tablet formulation for oral administration after reconstitution with water. The reference medicinal product is Panadol Soluble Tablets 500 mg (PL 00071/0072R granted 12 January 1982).

A maximum pack size of 16 tablets with GSL status is claimed for PL 16363/0127. This is acceptable.

A pack size of 32 tablets with P status is claimed for PL 16363/0194. This is acceptable.

The product name is in the acceptable format.

DRUG SUBSTANCE

Paracetamol is the subject of a Ph.Eur. monograph. The source of paracetamol is named and this source has a Certificate of Suitability. In view of the drug substance and the Certificate of Suitability the named source of paracetamol is considered acceptable and no further assessment is performed here.

The specification is supported by three Certificates of Analysis.

DRUG PRODUCT

Description and composition of the drug product

Composition of the soluble tablet is defined. Dissolution in water produces a lemon flavoured solution.

Pharmaceutical development

No bioequivalence studies are reported. However, as the product is dissolved in water prior to administration, the absence of a bioavailability study for this active and product may be considered acceptable.
Particle size control of the paracetamol is exercised in the drug substance specification.

**Manufacture, control and process validation**

A manufacturing formula is given for a suitable batch size. Manufacturing process is given both in the narrative and flow chart form.

Suitable in-process controls are exercised.

Manufacturing process validation is provided. Three full scale batches have been subjected to process validation at the named manufacturing site. Batch analysis of the three production scale batches indicate a satisfactory manufacturing process for intra and inter batches.

**Control of excipients**

Other ingredients are compendial grade being Ph.Eur. except for Simethicone Emulsion, which is USP, but contains components complying with Ph.Eur. Lactose monohydrate is considered to comply with BSE/TSE requirements. Lemon flavour H & R 213841 is non-compendial and for this qualitative composition and in-house specification is provided.

These specifications are supported by Certificates of Analysis for the specified batches of ingredients.

**Control of drug product**

A comprehensive finished product specification is provided that includes disintegration time, which is important for this type of product.

Analytical methods are provided with reference being made to Ph.Eur. where relevant.

**Reference standards or materials**

Satisfactory information on reference standards is provided.

**Container closure system**

Immediate packaging is a white polypropylene tube with polyethylene caps / stoppers with desiccant of white silica.

Specifications are provided for these packaging materials supported by Certificates of Analysis.

**Stability**

Stability data are provided on five batches of the drug product. Three laboratory scale batches were stored at ambient room temperature. Two commercial scale batches of tablets produced at the named manufacturing site were stored under ICH conditions of 25°C/60% RH, 40°C/75% RH and 30°C/60% RH as a back up. Batch histories are given and the named active source has been used in these stability batches. A stability protocol is provided.
Results indicate the product to be stable as little or no changes are observed on storage except for increase for LOD of the desiccant, which is to be expected, but remained within specification.

**PRODUCT PARTICULARS**

**Application Form**

An application form is provided.

**SPC**

A satisfactory SPC is provided.

**Labelling**

Colour mock-ups of tube and carton labelling are provided.

**Package Leaflet**

A colour mock-up of the leaflet is provided.

**GMP status**

This is satisfactory as a copy of the manufacturing licence is provided for the named site. The batch release site is Milpharm Ltd, UK.

**PHARMACEUTICAL EXPERT REPORT**

The report is adequate.

**PHARMACEUTICAL CONCLUSION**

That marketing authorisations should be granted.
PRECLINICAL ASSESSMENT

LICENCE No.: PL 16363/0127, 0194
PROPRIETARY NAME: Paracetamol 500mg Soluble Tablets
ACTIVE(S): Paracetamol Ph.Eur.
COMPANY NAME: Milpharm Limited
EC ARTICLE: 10.1 (a)(iii)
LEGAL STATUS: GSL, P

INTRODUCTION

These are national abridged application for soluble paracetamol tablets containing 500mg of the active ingredient paracetamol, claiming essential similarity to Panadol Soluble Tablets 500mg (PL 00071/0072R) first licensed in the UK on 12 January 1982.

The proposed product is intended for relief of mild to moderate pain including headache, migraine, backache, rheumatic and muscle pain, neuralgia, toothache and period pain as well as symptoms of colds and flu, including sore throat and fever.

The recommended daily dose for adults and children 12 years and over is two tablets every four to six hours, not exceeding eight tablets daily (MRDD of 4g paracetamol). The maximum recommended dose for children between 6-12 years of age is one tablet every four to six hours, not exceeding four tablets daily (MRDD of 2g paracetamol).

OVERVIEW

The pharmacology and toxicology of paracetamol are well established and will not be reiterated here. In the UK, paracetamol has been safely used at the maximum dose regimen for many years. The Expert’s review of the preclinical literature available does not raise any new safety concerns. Since there is ample data on the clinical safety of paracetamol, absence of preclinical studies with the proposed formulation is considered acceptable.

The proposed drug substance specification limits for the known related substances 4-chloroacetaniline and 4-aminophenol and any other impurities are in line with the European Pharmacopoeia (EP) specifications and are of no safety concern.

The proposed finished product specification limits for 4-aminophenol and for 4-chloroacetaniline are within those of BP specification for dispersible paracetamol and pose no safety concern.

All excipients of the proposed formulation are routinely used in oral pharmaceutical products and do not raise any safety concerns at the proposed limit and dose regimen.

PHARMACO-TOXICOLOGICAL EXPERT REPORT

A pharmaco-toxicological Expert Report is provided. This consists of an adequate summary of the pharmacology and toxicology of paracetamol with reference literature published between 1976-2000.

SUMMARY OF PRODUCT CHARACTERISTICS

Satisfactory.
PATIENT INFORMATION LEAFLET and CARTON LABEL

Acceptable.

CONCLUSIONS

There are no preclinical objections to the grant of marketing authorisations for Paracetamol 500mg Soluble Tablets.
CLINICAL ASSESSMENT

LICENCE No.: PL 16363/0127, 0194
PROPRIETARY NAME: Paracetamol 500mg Soluble Tablets
ACTIVE(S): Paracetamol Ph.Eur.
COMPANY NAME: Milpharm Limited
EC ARTICLE: 10.1 (a)(iii)
LEGAL STATUS: GSL, P

These are national abridged application for soluble paracetamol tablets containing 500mg of the active ingredient paracetamol, claiming essential similarity to Panadol Soluble Tablets 500mg (PL 00071/0072R) first licensed in the UK on 12 January 1982.

EFFICACY

No new data has been submitted and none is required for this application.

SAFETY

No new data has been submitted and none is required for this application.

Safety is reviewed in the Clinical Expert Report. The safety profile of paracetamol has been well-established by many years of clinical use.

EXPERT REPORT

The report is written by a medically qualified expert and is satisfactory.

SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

The SPC is satisfactory.

PATIENT INFORMATION LEAFLET (PIL)

The PIL is in line with the SPC and is satisfactory.

LABELLING

The labelling is satisfactory.

CONCLUSIONS

The grounds for this application are considered adequate. The product literature is approved.

Grant of a marketing authorisation is recommended.
OVERALL CONCLUSION AND RISK-BENEFIT ASSESSMENT

QUALITY

The important quality characteristics of Paracetamol 500mg Soluble Tablets are well defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRECLINICAL

No new preclinical data were submitted and none are required for applications of this type.

EFFICACY

The SPC, PIL and labelling are satisfactory and consistent with those of Panadol 500mg Soluble Tablets.

RISK-BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. Extensive clinical experience with paracetamol is considered to have demonstrated the therapeutic value of the compound. The risk-benefit assessment is therefore considered to be favourable.
**PARACETAMOL 500MG SOLUBLE TABLETS**

**PL 16363/0127**

**STEPS TAKEN FOR ASSESSMENT**

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<td>1</td>
<td>The MHRA received the marketing authorisation application for Paracetamol 500mg Soluble Tablets on 24 July 2002.</td>
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**PL 16363/0194**

**STEPS TAKEN FOR ASSESSMENT**

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PARACETAMOL 500MG SOLUBLE TABLETS

PL 16363/0127
PL 16363/0194

STEPS TAKEN AFTER AUTHORISATION - SUMMARY

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SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Paracetamol 500mg Soluble Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Soluble tablet contains:

Paracetamol 500mg

For excipients, see 6.1

3. PHARMACEUTICAL FORM

Soluble Tablet

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

Paracetamol 500mg Tablets is a mild analgesic and antipyretic and is recommended for the treatment of most painful and febrile conditions, for example, headache including migraine and tension headaches, toothache, neuralgia, backache, rheumatic and muscle pains, dysmenorrhoea, sore throat and for relieving the fever, aches and pains of colds and flu.

4.2. Posology and Method of Administration

Adults and elderly:
1-2 tablets dissolved in a glass of water up to 4 times a day. These doses should not be repeated more frequently than every 4 hours and not more than 4 doses should be given in any 24 hour period. Not recommended for children under 12 years of age. Oral administration only.

4.3. Contra-indications

Hypersensitivity to paracetamol or any of the other constituents.
4.4. Special Warnings and Precautions for Use

Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment. The hazard of overdose is greater in those with non-cirrhotic alcoholic liver disease.

Do not exceed the stated dose.

Patients should be advised to consult their doctor if their headaches become persistent.

Patients should be advised not to take other paracetamol-containing products concurrently.

If symptoms persist, consult your doctor.

Keep out of the reach of children.

Pack Label:
Immediate medical advice should be sought in the event of an overdose, even if you feel well.

Do not take with other paracetamol-containing products.

Patient Information Leaflet:
Immediate medical advice should be sought in the event of an overdose even if you feel well, because of the risk of delayed, serious liver damage.

4.5. Interactions with other Medicaments and other forms of Interaction

The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by cholestyramine. The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

4.6. Pregnancy and Lactation

Epidemiological studies in human pregnancy have shown no ill effects due to paracetamol used in the recommended dosage, but patients should follow the advice of the doctor regarding its use.

Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breast feeding.

4.7. Effects on Ability to Drive and Use Machines

No special comment. Unlikely to produce an effect.
4.8. Undesirable Effects

Adverse effects of paracetamol are rare but hypersensitivity, including skin rash, may occur. There have been very rare reports of blood dyscrasias including thrombocytopenia and agranulocytosis but these were not necessarily causally related to paracetamol.

4.9. Overdose

Symptoms of overdosage:

Pallor, anorexia, nausea, vomiting and abdominal pain are frequent early symptoms of paracetamol overdose.

Hepatic necrosis is a dose-related complication of paracetamol overdose. Hepatic enzymes may become elevated and prothrombin time prolonged within 12 to 48 hours but clinical symptoms may not be apparent for 1 to 6 days after ingestion. Toxicity is likely in subjects who have taken single doses of 10 g (150 mg/kg) or more. It is considered that excess quantities of toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are ingested) become irreversibly bound to liver tissue.

Paracetamol hepatotoxicity is directly dependent on the plasma concentration related to time. Plasma concentrations above 1.2 mmol/l at 4 hours, 0.6 mmol/l at 8 hours and 0.3 mmol/l at 12 hours are criteria for treatment with acetylcysteine to prevent irreversible liver damage.

Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, coma and death. Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported.

In paracetamol overdose with liver cell damage, paracetamol half-life is often prolonged from around 2 hours in normal adults to 4 hours or longer. However liver cell damage has been found in patients with a paracetamol half life less than 4 hours. Renal failure due to acute tubular necrosis may follow paracetamol-induced fulminant hepatic failure. The incidence of this is, however, no more frequent in these patients than in others with fulminant hepatic failure from other causes.

Therapeutic measures in overdosage:

Immediate treatment is essential in the management of paracetamol overdose. Despite a lack of significant early symptoms, patients should be referred to hospital urgently for immediate medical attention and any patient who had ingested around 7.5 g or more of paracetamol in the preceding 4 hours should undergo gastric lavage. Administration of oral methionine or intravenous N-acetylcysteine which may have beneficial effect up to at least 48 hours after overdose, may be required. General supportive measures must be available.
5 PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic Properties

ATC Name. Analgesics
ATC Code. N02
Paracetamol has analgesic and antipyretic effects similar to those of aspirin and is useful in the treatment of mild to moderate pain. It has weak anti-inflammatory effects.

5.2. Pharmacokinetic Properties

Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract. Peak plasma concentrations are reached 30-90 minutes post dose and the plasma half-life is in the range of 1 to 3 hours after therapeutic doses. Drug is widely distributed throughout most body fluids. Following therapeutic doses 90-100% of the drug is recovered in the urine within 24 hours almost entirely following hepatic conjugation with glucuronic acid (about 60%), sulphuric acid (about 35%) or cysteine (about 3%). Small amounts of hydroxylated and deacetylated metabolites have been detected. Children have less capacity for glucuronidation of the drug than do adults. In overdosage there is increased N-hydroxylation followed by glutathione conjugation. When the latter is exhausted, reaction with hepatic proteins is increased leading to necrosis.

5.3. Preclinical Safety Data

There are no pre-clinical data of relevance to the prescriber, which are additional to those already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1. List of Excipients
Citric acid
Sodium sulphate
Lactose monohydrate
Sodium hydrogen carbonate
Povidone
Simethicone
Saccharin sodium
Lemon flavour, containing citral, citric acid, ethyl alcohol, lemon oil, lime oil, alphatocopherol, triacetine, maltodextrin, gum arabic and sucrose
Macrogol 6000
6.2. Incompatibilities

None known

6.3. Shelf Life

3 years

6.4. Special Precautions for Storage

Do not store above 25°C. Store in the original container. Keep the container tightly closed at dry place.

6.5. Nature and Contents of Container

Polypropylene tube with polyethylene stopper containing silica gel as desiccant. The tubes are packed into an outer carton. Pack sizes: 6, 12 and 16 tablets

6.6. Instruction for Use/Handling

Dissolve tablets in a glass of water prior to intake. Sodium content: approximately 392 mg per tablet.

7 MARKETING AUTHORITY NUMBER

Milpharm Limited
298 Regents Park Road
Marlborough House
Finchley
London N3 2UA
UK

8 MARKETING AUTHORITY NUMBER

PL 16363/0127
9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23/05/2006

10 DATE OF REVISION OF THE TEXT

23/05/2006
1. NAME OF THE MEDICINAL PRODUCT
Paracetamol 500mg Soluble Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each Soluble tablet contains Paracetamol 500mg
Also contains lactose monohydrate, sodium; For excipients, see 6.1

3. PHARMACEUTICAL FORM
Soluble Tablets
Round, biplane, white or off-white tablets with facets on both sides

4. CLINICAL PARTICULARS

4.1. Therapeutic indications
Paracetamol 500mg Tablets is a mild analgesic and antipyretic and is recommended
for the treatment of most painful and febrile conditions, for example, headache
including migraine and tension headaches, toothache, neuralgia, backache, rheumatic
and muscle pains, dysmenorrhoea, sore throat and for relieving the fever, aches and
pains of colds and flu.

4.2. Posology and method of administration

Adults and elderly:
1-2 tablets dissolved in a glass of water up to 4 times a day.
These doses should not be repeated more frequently than every 4 hours and not more
than 4 doses should be given in any 24hour period.
Not recommended for children under 12 years of age.
Oral administration only.

4.3. Contraindications
Hypersensitivity to paracetamol or any of the other constituents
4.4. Special warnings and precautions for use

Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment. The hazard of overdose is greater in those with non-cirrhotic alcoholic liver disease.
Do not exceed the stated dose.
Patients should be advised to consult their doctor if their headaches become persistent.
Patients should be advised not to take other paracetamol-containing products concurrently.
If symptoms persist, consult your doctor.
Keep out of the reach and sight of children.
Sodium content: approximately 392 mg per tablet.
This product contains lactose; patient with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
Pack Label:
Immediate medical advice should be sought in the event of an overdose, even if you feel well.
Do not take with other paracetamol-containing products.
Patient Information Leaflet:
Immediate medical advice should be sought in the event of an overdose even if you feel well, because of the risk of delayed, serious liver damage.

4.5. Interactions with other medicinal products and other forms of interaction

The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by cholestyramine. The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

4.6. Pregnancy and lactation

Epidemiological studies in human pregnancy have shown no ill effects due to paracetamol used in the recommended dosage, but patients should follow the advice of the doctor regarding its use.
Paracetamol is excreted in breast milk but not in a clinically significant amount.
available published data do not contraindicate breast feeding.

4.7. Effects on ability to drive and use machines

No special comment. Unlikely to produce an effect.
4.8. Undesirable effects

Adverse effects of paracetamol are rare but hypersensitivity, including skin rash, may occur. There have been very rare reports of blood dyscrasias including thrombocytopenia and agranulocytosis but these were not necessarily causally related to paracetamol.

4.9. Overdose

**Symptoms of overdosage:**
Pallor, anorexia, nausea, vomiting and abdominal pain are frequent early symptoms of paracetamol overdosage.
Heaptic necrosis is a dose-related complication of paracetamol overdose. Hepatic enzymes may become elevated and prothrombin time prolonged within 12 to 48 hours but clinical symptoms may not be apparent for 1 to 6 days after ingestion. Toxicity is likely in subjects who have taken single doses of 10 g (150 mg/kg) or more. It is considered that excess quantities of toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are ingested) become irreversibly bound to liver tissue.
Paracetamol hepatotoxicity is directly dependent on the plasma concentration related to time. Plasma concentrations above 1.2 mmol/l at 4 hours, 0.6 mmol/l at 8 hours and 0.3 mmol/l at 12 hours are criteria for treatment with acetylcysteine to prevent irreversible liver damage.
Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, coma and death. Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported.
In paracetamol overdosage with liver cell damage, paracetamol half-life is often prolonged from around 2 hours in normal adults to 4 hours or longer. However liver cell damage has been found in patients with a paracetamol half life less than 4 hours.
Renal failure due to acute tubular necrosis may follow paracetamol-induced fulminant hepatic failure. The incidence of this is, however, no more frequent in these patients than in others with fulminant hepatic failure from other causes.

**Therapeutic measures in overdosage:**
Immediate treatment is essential in the management of paracetamol overdose. Despite a lack of significant early symptoms, patients should be referred to hospital urgently for immediate medical attention and any patient who had ingested around 7.5 g or more of paracetamol in the preceding 4 hours should undergo gastric lavage.
Administration of oral methionine or intravenous N-acetylcysteine which may have beneficial effect up to at least 48 hours after overdose, may be required. General supportive measures must be available.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

**Pharmacotherapeutic group:** Anilides

MHRA: PAR – Paracetamol 500mg Soluble Tablets PL 16363/0127, 0194
ATC Code: N02B E01

Paracetamol has analgesic and antipyretic effects similar to those of aspirin and is useful in the treatment of mild to moderate pain. It has weak anti-inflammatory effects.

5.2. Pharmacokinetic properties

Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract. Peak plasma concentrations are reached 30-90 minutes post dose and the plasma half-life is in the range of 1 to 3 hours after therapeutic doses. Drug is widely distributed throughout most body fluids. Following therapeutic doses 90-100% of the drug is recovered in the urine within 24 hours almost entirely following hepatic conjugation with glucuronic acid (about 60%), sulphuric acid (about 35%) or cysteine (about 3%). Small amounts of hydroxylated and deacetylated metabolites have been detected. Children have less capacity for glucuronidation of the drug than do adults. In overdosage there is increased N-hydroxylation followed by glutathione conjugation. When the latter is exhausted, reaction with hepatic proteins is increased leading to necrosis.

5.3. Preclinical safety data

There are no pre-clinical data of relevance to the prescriber, which are additional to those already included in other sections of the SPC.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Anhydrous citric acid
Anhydrous sodium sulphate
Lactose monohydrate
Sodium bicarbonate
Povidone k-25
Simethicone emulsion (dry)
Saccharin sodium
Lemon flavour; containing citral, citric acid, ethyl alcohol, lemon oil, lime oil, alpha-tocopherol, triacetine, maltodextrin, gum arabic and sucrose
Macrogol 6000

6.2. Incompatibilities

Not applicable.
6.3. Shelf life

3 years

6.4. Special precautions for storage

Do not store above 25°C. Store in the original package. Keep the tablet container tightly closed.

6.5. Nature and contents of container

Polypropylene tablet container with polyethylene stopper containing silica gel as desiccant. 16 Soluble tablets are packed in one tablet container. Two such tablet containers are packed into an outer carton.
Pack size: 32 tablets

6.6. Instruction for use and handling (, and disposal)

Dissolve tablet in a glass of water prior to intake.

7. MARKETING AUTHORISATION HOLDER

Milpharm Limited
298 Regents Park Road
Marlborough House
Finchley
London N3 2UA, UK

8. MARKETING AUTHORISATION NUMBER

PL 16363/0194

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23/05/2006
DATE OF REVISION OF THE TEXT

23/05/2006
Patient Information Leaflet

PARACETAMOL 500MG SOLUBLE TABLETS

PL 16363/0127
Read all of this leaflet carefully because it contains important information for you.
This medicine is available without prescription. Nevertheless you still need to use Paracetamol 500mg Soluble tablets carefully to get the best results from it.
- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- You must see a doctor if your symptoms worsen or do not improve after 3 days.

**WHAT ARE PARACETAMOL 500MG SOLUBLE TABLETS AND WHAT ARE THEY USED FOR?**

What are Paracetamol 500mg Soluble Tablets?
These tablets contain paracetamol which is an analgesic (pain-killer) and antipyretic (brings down the body temperature in case of fever).

What are they used for?
Paracetamol Soluble Tablets are used for headache, migraine, tension headaches, toothache, neuralgia, rheumatic and muscle pain, period pain, sore throat and for relieving the fever, aches and pains of cold and flu.

**THE LEAFLET CONTAINS INFORMATION ON:**
- What are Paracetamol 500mg Soluble Tablets and what are they used for?
- Information to read before taking Paracetamol 500mg Soluble Tablets?
- How to take your tablets?
- Can your tablets have any side effects?
- Storing your tablets

**INFORMATION TO READ BEFORE USING PARACETAMOL 500MG SOLUBLE TABLETS**

Do not take Paracetamol 500mg Soluble Tablets:
- If you are allergic or sensitive to paracetamol
- If you are allergic or sensitive to any other ingredient of this product
- If you are a child below 12 years of age.
Take special care with Paracetamol 500mg Soluble Tablets:
- If you suffer from severe liver disease
- If you suffer from severe kidney disease

Please consult your doctor if any of the above statements are applicable to you.

Taking Paracetamol 500mg Soluble Tablets with other medication
Please see your doctor before taking your tablets if you are taking:
- Metoclopramide or domperidone – used for nausea and vomiting
- Cholestryamine – used for high blood cholesterol
- Anti-coagulants (blood-thinning drugs) like warfarin and you need to take Paracetamol 500mg Soluble tablets regularly. However, occasional doses can be taken

WARNING:
1. PLEASE DO NOT TAKE WITH ANY OTHER PARACETAMOL-CONTAINING PRODUCTS.
2. IF SYMPTOMS PERSIST, CONSULT YOU DOCTOR

Immediate medical advice should be sought in the event of an overdose even if you feel well.

Pregnancy:
Please consult your doctor for advice before taking these tablets.

Breast-feeding
You can take Paracetamol 500mg Soluble Tablets whilst breast-feeding

Effect on the ability to drive and use machines:
Your tablets are unlikely to have any effect on your ability to drive and use machines

Important information about some of the ingredients of Paracetamol 500mg Soluble Tablets:
Each tablet contains 392mg of sodium. THESE TABLETS MAY BE HARMFUL FOR PEOPLE ON LOW SODIUM DIET

HOW TO TAKE YOUR TABLETS?
Please dissolve your tablet(s) in a glass of water before taking. The recommended doses are as follows:

**Adults (including elderly) and children over 12 years**
1-2 tablets every four to six hours as required. Do not take more than 8 tablets in 24 hours
DO NOT EXCEED THE STATED DOSE

Consult your doctor if symptoms persist.

If you take too many tablets
Immediate medical advise should be sought in the event of an overdose even if you feel well, because of the risk of delayed, serious liver damage.

CAN YOUR TABLETS HAVE ANY SIDE EFFECTS?

Like all other medicines, Paracetamol 500mg Soluble Tablets can have side effects. Side effects are usually mild and may include skin rashes and other allergic reactions occasionally. Very rarely there have been reports of blood disorders but these were not necessarily caused by paracetamol. These effects should go away once you stop taking your tablets. In case you are concerned about these effects or you notice any side effects not mentioned in this leaflet, please consult your doctor or pharmacist.

STORING YOUR TABLETS.

- Keep all medicines away from the reach and sight of children
- On the label you will find a date after which the medicine is no longer fit for use. Do not use this medicine after this date
- Do not store above 25°C. Store in original container. Keep the container tightly closed in dry place.
- Store away from heat and direct sunlight
- Do not store in bathroom, near the kitchen sink, or in damp places. Heat or moisture may cause the medicine to break down

FURTHER INFORMATION

The name of your medicine is Paracetamol 500mg Soluble Tablets. These are white, biplane tablets with facets on both sides. Each tablet contains Paracetamol 500mg. Other ingredients are citric acid anhydrous, sodium sulphate anhydrous, lactose monohydrate, sodium hydrogen carbonate, povidone K25, simeticone, saccharin sodium, lemon flavour H & R 213 841 and macrogol 6000

Paracetamol 500mg Soluble Tablets are available in the tube pack of 8, 12 and 16 tablets.

The marketing authorisation holder: Milpharm Limited, Marlborough House, 298, Regents Park Road, Finchley, London N3 2UA, United Kingdom
The tablets are manufactured by: Milpharm Limited, Marlborough House, 298, Regents Park Road, Finchley, London N3 2UA, United Kingdom

Date of preparation: March 2006
PARACETAMOL 500MG SOLUBLE TABLETS

PL 16363/0194
This medicine is available without prescription, for you to treat a mild illness without a doctor’s help. Nevertheless, you still need to use Paracetamol 500mg Soluble Tablets carefully to get the best results from it.

- Keep this leaflet. You may need to read this again.
- Ask your pharmacist if you need more information or advice.
- You must see a doctor if your symptoms worsen or do not improve after 3 days.

THE LEAFLET CONTAINS INFORMATION ON:

- What are Paracetamol 500mg Soluble Tablets and what are they used for?
- Information to read before taking Paracetamol 500mg Soluble Tablets?
- How to take your tablets?
- Can your tablets have any side effects?
- Storing your tablets?

The name of your medicine is Paracetamol 500mg Soluble Tablets. These are white, biplane tablets with facets on both sides. Each tablet contains Paracetamol 500mg. Other ingredients are citric acid anhydrous, sodium sulphate anhydrous, lactose monohydrate, sodium hydrogen carbonate, povidone K25, simethicone, saccharin sodium, lemon flavour H & R 213 841 (containing citral, citric acid, ethyl alcohol, lemon oil, lime oil, alphatocopherol, triacetin, maltodextrin, gum arabic and sucrose) and macrogel 5000.

The marketing authorisation holder: Milpharm Limited, Marlborough House, 298, Regents Park Road, Finchley, London N3 2UA, United Kingdom.

The tablets are manufactured by: Milpharm Limited, Marlborough House, 298, Regents Park Road, Finchley, London N3 2UA, United Kingdom.

WHAT ARE PARACETAMOL 500MG SOLUBLE TABLETS AND WHAT ARE THEY USED FOR?

What are Paracetamol 500mg Soluble Tablets?
These tablets contain paracetamol which is an analgesic (pain-killer) and antipyretic (brings down the body temperature in case of fever). Paracetamol 500mg Soluble Tablets are available in the tube pack of 32 tablets (2x16 tablets).

**What are they used for?**
Paracetamol Soluble Tablets are used for headache, migraine, tension headaches, toothache, neuralgia, rheumatic and muscle pain, period pain, sore throat and for relieving the fever, aches and pains of cold and flu.

**INFORMATION TO READ BEFORE USING PARACETAMOL 500MG SOLUBLE TABLETS**

**Do not take Paracetamol 500mg Soluble Tablets:**
- If you are allergic or sensitive to paracetamol
- If you are allergic or sensitive to any other ingredient of this product
- If you are a child below 12 years of age.

**Take special care with Paracetamol 500mg Soluble Tablets:**
- If you suffer from severe liver disease
- If you suffer from severe kidney disease

Please consult your doctor if any of the above statements are applicable to you.

**WARNING:**
1. PLEASE DO NOT TAKE WITH ANY OTHER PARACETAMOL-CONTAINING PRODUCTS.
2. IF SYMPTOMS PERSIST, CONSULT YOUR DOCTOR

Immediate medical advice should be sought in the event of an overdose even if you feel well.

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

**Pregnancy:**
Please consult your doctor for advice before taking these tablets.

**Breast-feeding**
You can take Paracetamol 500mg Soluble Tablets whilst breast-feeding

**Effect on the ability to drive and use machines:**
Your tablets are unlikely to have any effect on your ability to drive and use machines

**Important information about some of the ingredients of Paracetamol 500mg Soluble Tablets:**
Each tablet contains 392mg of sodium. THESE TABLETS MAY BE HARMFUL FOR PEOPLE ON LOW SODIUM DIET

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Please see your doctor before taking your tablets if you are taking:

- Metoclopramide or domperidone – used for nausea and vomiting
- Cholestryamine – used for high blood cholesterol
- Anti-coagulants (blood-thinning drugs) like warfarin and you need to take Paracetamol 500mg Soluble tablets regularly. However, occasional doses can be taken

**HOW TO TAKE YOUR TABLETS?**

Please dissolve your tablet(s) in a glass of water before taking. The recommended doses are as follows:

*Adults (including elderly) and children over 12 years*

1-2 tablets every four to six hours as required. Do not take more than 8 tablets in 24 hours

**DO NOT EXCEED THE STATED DOSE**

Consult your doctor if symptoms persist.

**If you take too many tablets**

Immediate medical advise should be sought in the event of an overdose even if you feel well, because of the risk of delayed, serious liver damage.

**CAN YOUR TABLETS HAVE ANY SIDE EFFECTS?**

Like all other medicines, Paracetamol 500mg Soluble Tablets can have side effects.

Side effects are usually mild and may include skin rashes and other allergic reactions occasionally. Very rarely there have been reports of blood disorders but these were not necessarily caused by paracetamol. These effects should go away once you stop taking your tablets.

In case you are concerned about these effects or you notice any side effects not mentioned in this leaflet, please consult your doctor or pharmacist.

**STORING YOUR TABLETS.**

- Keep all medicines away from the reach and sight of children
- Do not store above 25°C. Store in original container. Keep the container tightly closed.
- On the label you will find a date after which the medicine is no longer fit for use. Do not use this medicine after this date
- Store away from heat and direct sunlight
- Do not store in bathroom, near the kitchen sink, or in damp places. Heat or moisture may cause the medicine to break down

Date of preparation: April 2006

PL 16363/0194
Labels/Packaging
PARACETAMOL 500MG SOLUBLE TABLETS

PL 16363/0127

How to take your tablets
Adoles (including adolescents)
Take 1-2 tablets dissolved in a glass of water every four to six hours. Do not take more than 8 tablets in 24 hours.

Not recommended for children below 12 years of age

DO NOT EXCEED THE STATED DOSE

Immediate medical advice should be sought in the event of an overdose, even if you feel well.

Do not take with other paracetamol-containing products

Please consult your doctor
• Before taking these tablets if you have severe kidney or liver problem
• After taking these tablets, if the symptoms persist