NHS FORTH VALLEY
Proton Pump Inhibitor (PPI) Prescribing- Step Down in Long term Use Guidance

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Author / Contact Laura Lee
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<tr>
<th>Contributing Authors:</th>
<th>Laura Lee, Pauline Morrison, Gillian Cook, Dr Stuart Paterson, Dr Leslie Cruickshank</th>
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<tr>
<td>Consultation Process:</td>
<td>Primary Care Pharmacists, Forth Valley Primary Care Prescribing Group</td>
</tr>
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<td>Distribution:</td>
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**Introduction**
This document aims to help prescribers weigh up the relative risks/benefits of long term proton pump inhibitor (PPI) use and give guidance on which categories of patients can be appropriately considered for a reduction/discontinuation of their current PPI dose and which categories of patients in whom it would not be appropriate to reduce/stop their PPI.

This guidance relates to patients on long-term, ‘maintenance’ doses of PPIs after all initial diagnoses, investigations and treatment courses are complete. It covers undiagnosed dyspeptic or reflux symptoms; proven non-ulcer dyspepsia or symptoms of gastro-oesophageal reflux with no changes on endoscopy; gastritis, duodenitis, peptic ulcer; and oesophagitis A/B.

It **excludes** patients with Barrett’s, oesophagitis grade C/D, oesophageal cancer, Zollinger-Ellison disease, oesophageal stricture/ulceration, oesophageal or gastric varices in banding programme, gastric cancer; any patient under secondary care follow up.

This guidance is **not** intended to serve as a standard of care or be applicable in every situation. Decisions regarding the treatment of individual patients must be made by the clinician in light of that patient’s presenting clinical condition and with reference to current good medical practice.

Due to the known potential adverse effects of PPIs and the benefits that PPIs bring to patients in terms of symptom management, the risks and benefits need to be weighed up for each patient.

**Scope**
This guidance is applicable to all Independent Prescribers working in General Practice in NHS Forth Valley.

**1. Long Term Side Effects of Proton Pump Inhibitors**
Proton Pump Inhibitors (PPIs) are well tolerated. Their safety and efficacy can lead to overuse, inappropriate dosage or excessive duration of treatment. However, there are risks that may be elevated when PPIs are used regularly and in the long term.

Low magnesium levels have been reported in patients taking long term PPIs. The MHRA \(^1\) recommends consideration of serum-magnesium measurement before and during prolonged PPI treatment, especially when used with other drugs that cause hypomagnesaemia (eg diuretics) or with digoxin.

PPIs, especially when used in high doses for long durations (>1 year), may modestly increase the risk of hip, wrist and spine fracture. Observational studies suggest that this may increase the overall risk of fracture by 10-40%\(^2\). Other risk factors are likely to play a part in this Therefore, patients at risk of osteoporosis should have an adequate intake of calcium and vitamin D and receive other preventative therapy, if necessary\(^3\).

There is increasing evidence that long term use of PPIs may be associated with increased risks of enteric infections such as C. difficile \(^4,5\),

In order to minimise any potential for side effects, the unnecessary use of PPIs should be minimised by the regular review of all patients- especially those on long-term treatment. Consider if PPI benefit outweighs risks for all patients but especially for those more likely to be at increased risk of these longer term side effects such as the frail elderly.
All PPIs have been studied as on-demand (taking a medicine “as required” or “as needed” by the patient in response to symptoms) therapy for recurrent dyspepsia, but only rabeprazole and esomeprazole are currently licensed for this indication. It is the view of local experts that at the point patients are being reduced from the lowest available commercial strength that “on-demand” prescribing is appropriate for all available PPIs.

2. PPI Step Down/Step Off

Patients Not Suitable for Step Down/Step Off of PPI Dose
- Patients with Barrett's, oesophagitis grade C/D, oesophageal cancer, Zollinger-Ellison disease, oesophageal stricture/ulceration, oesophageal or gastric varices in banding programme, gastric cancer; any patient under secondary care follow up.
- Patients requiring long term gastro-protection should remain on a licensed dose of PPI.

Patients Where Step Down/Step off of PPI Treatment Should be Considered
This applies to patients on long-term, ‘maintenance’ doses of PPIs after all initial diagnoses, investigations and treatment courses are complete and are not requiring gastro-protection
- Patients with uninvestigated dyspeptic symptoms including symptoms of reflux
- Patients with proven non–ulcer dyspepsia (functional) with NO changes on endoscopy ie no oesophagitis (any grade), atypia, dysplasia, strictures or ulceration
- Patients with symptoms of gastro-oesophageal reflux without oesophagitis on endoscopy
- Grade A/B oesophagitis. However, patients with ongoing symptoms will need to remain on the lowest effective dose of PPI.
- Peptic Ulcer Disease

How to step down
General rules:
- Ensure good symptom control on current dose (if symptom control is poor on current dose – step down is not appropriate. Consider alternative diagnosis/treatment).
- Consider: GI irritant medicines eg NSAIDs; or drugs known to lower the oesophageal sphincter pressure and therefore potentially contributing to symptoms of GORD eg theophylline, nitrates, calcium-channel blockers, beta-blockers, alpha-blockers, benzodiazepines, tricyclic antidepressants, and anticholinergics.; H pylori status; seeking specialist advice /alternative diagnosis or re-referral especially if on double dose as per table 1)
- Consider H. pylori status
- Offer lifestyle advice as appropriate as per PIL/Appendix 1 Patient Information Leaflet
  - keep to a health weight
  - don’t smoke
  - eat and drink alcohol in moderation
  - avoid foods that give symptoms
  - avoid anti-inflammatory painkillers
  - reduce stress
For those with heartburn or reflux

- avoid tight belts of clothing
- eat your evening meal well before bedtime and avoid bending down or lying flat after meals
- raise the height of the bed by 4-6 inches using blocks under the legs of the bed

- Explain potential for rebound symptoms. Taking a PPI for more than a few weeks can lead to a temporary increase in the secretion of stomach acid although there are no data that support acid rebound as a clinical problem in patients. For this reason, some people may find that their symptoms of heartburn and dyspepsia may worsen when they try to stop taking a PPI.
- Offer follow up/review at least annually

**Suggested step down ladders for commonly prescribed PPIs:**

There is no national guidance on how to step down PPI doses. Local advice suggests the following approach – using omeprazole as an example – is a reasonable example of step down. The aim would be that the patient is reduced to the lowest effective dose. Refer to table 1 for equivalence doses to transfer this step down example to other PPIs.

Omeprazole 40mg BD
   To
Omeprazole 20mg BD for one month
   To
Omeprazole 20mg OD for one month
   To
Omeprazole 10mg OD for one month
   To
Omeprazole 10mg prn for symptom control for one month then stop if possible

see appendix 2 more information

**Dose Equivalences**

Table 1 below give approximate dosage equivalences for the purposes of stepping down treatment

<table>
<thead>
<tr>
<th>PPI</th>
<th>Low Dose (on-demand dose)</th>
<th>Full/Standard Dose</th>
<th>Double Dose</th>
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<tbody>
<tr>
<td>Omeprazole</td>
<td>10mg daily</td>
<td>20mg once a day</td>
<td>40mg daily (20mg twice a day); or 40mg twice a day*</td>
</tr>
<tr>
<td>Lansoprazole</td>
<td>15mg once a day</td>
<td>30mg once a day</td>
<td>30mg twice a day</td>
</tr>
<tr>
<td>Pantoprazole</td>
<td>20mg once a day</td>
<td>40mg once a day</td>
<td>40mg twice a day</td>
</tr>
<tr>
<td>Rabeprazole</td>
<td>10mg once a day</td>
<td>20mg once a day</td>
<td>20mg twice a day</td>
</tr>
<tr>
<td>Esomeprazole</td>
<td>Not available</td>
<td>20mg once a day</td>
<td>40mg daily (20mg twice a day); or 40mg twice a day*</td>
</tr>
</tbody>
</table>
*higher doses used severe oesophagitis (6)

An antacid or antacid/alginate can be considered for breakthrough symptoms of dyspepsia. Antacid/alginate combination may be helpful in patients with symptoms of gastro-oesophageal reflux.

Formulary choice of antacid is co-magaldrox. Formulary choice of antacid/alginate combination is Peptac(R).

Gastroprotection
The Clinical Knowledge Summaries covers the area of gastroprotection in detail and covers those patients at increased risk of gastro-intestinal effects from NSAIDs http://cks.nice.org.uk/nsaids-prescribing-issues#!scenariorecommendation:3 and antiplatelets. http://cks.nice.org.uk/antiplatelet-treatment#!scenariorecommendation:3

References

1. MHRA Drug Safety update- Proton Pump Inhibitors in long-term use:reports of hypomagnesaemia Vol 5, issue 9 April 2012
3. Losec 20mg Summary of Product Characteristics
5. BNF No 67 March-September 2014
6. Draft Dyspepsia and Gastro-oesophageal Reflux\Disease. NICE April2014
What happens if I take a PPI for more than a few weeks?
If you take a PPI for more than a few weeks, your stomach can increase its capacity to make acid, so that when the PPI is stopped, acid levels may be higher than before it was started.

For this reason, some people find that they get worse heartburn or dyspepsia when they try to stop taking a PPI, especially if they have been taking it for a long time.

How do I stop my PPI?
If you have been taking a PPI for more than eight weeks, we advise that you stop slowly. If you are on a high dose, ask your GP to prescribe a lower dose and take this dose daily for four weeks.

e.g.
Lansoprazole 30mg → 15mg
Omeprazole 40mg → 20mg → 10mg

When you have reached the lowest dose, you may be able to stop taking your PPI treatment every day. Talk to your doctor about which of the three ‘step down’ options described overleaf would suit you best.

How can I avoid dyspepsia?
- Don’t smoke
- Eat meals at regular times
- Eat and drink in moderation
- Avoid foods that give you symptoms
- Avoid anti-inflammatory painkillers (ask your pharmacist or doctor which painkillers are safe to take)
- Reduce stress - include some physical activity or relaxation every day.

How can I avoid heartburn?
- Try and keep to a healthy weight
- Cut back caffeine, alcohol, fatty foods
- Avoid tight belts or clothing
- Eat your evening meal well before bedtime and avoid bending down or lying flat after meals
- Raise the head of your bed by 10 to 15cm (4-6 inches) using blocks under the legs of your bed.

Adapted from the NHS Lothian Joint Formulary Patient Information Leaflet. 2012.
Introduction

Heartburn is a painful burning sensation felt in the chest behind the breast bone. Dyspepsia is described as pain or discomfort in the stomach or upper abdomen.

What are Proton Pump Inhibitors?

Proton Pump Inhibitors (often called PPIs) are a type of medicine used to treat heartburn and dyspepsia. The PPI medicines recommended for use in Forth Valley are called:
- omeprazole
- lansoprazole

How do PPIs work?

PPIs work by reducing the amount of acid that your stomach makes. By lowering acid levels they reduce the pain or discomfort you feel in your stomach or chest.

This reduction in acid also allows your body to heal any inflammation or ulcers that might have developed, usually within a few weeks of starting treatment.

Do PPIs have any side effects?

The most common side effects include constipation, diarrhoea, wind, nausea, vomiting and headaches. By lowering levels of acid in the stomach PPIs may
- interfere with the absorption of certain nutrients which may increase the risk of developing osteoporosis (a condition that affects bones) and fractures
- increase the risk of certain gastrointestinal (stomach and intestine) infections e.g. Clostridium difficile

Starting PPI treatment

For many people, only a short course of treatment is needed. To begin with, a PPI is usually prescribed at the full dosage for four weeks. If your symptoms continue, then another four weeks of treatment may be prescribed. After this, most people find that their heartburn or dyspepsia is better. However, it is common for these symptoms to come back again, maybe several months later.

Step down

After the initial course, treatment will be ‘stepped down’ to minimise the potential to develop side effects to one of the following three options:

1. ’Take when needed’ treatment
A PPI is prescribed for you to take only when you have heartburn or dyspepsia. When the symptoms have been relieved (often after a few days) you stop taking the PPI.

2. Short courses of treatment
If your symptoms return, your doctor will prescribe another short course of PPI treatment (usually for 2-4 weeks).

3. Low dose treatment
The dose of PPI is reduced to the lowest effective dose, or a different medicine is used to keep your symptoms at bay.

During step down, you may find that your symptoms return. It can be helpful to ask your pharmacist or doctor for a type of medicine called an ‘alginate’ to relieve heartburn, or an antacid to relieve dyspepsia.
Appendix 2

Long term dosage step down management plan after initial diagnosis, investigation and treatment with PPIs and successful eradication of H. pylori where applicable

If at any point alarm symptoms develop then patient should be referred for urgent endoscopy

This flow chart is relevant to patients with undiagnosed dyspeptic or reflux symptoms; proven non ulcer dyspepsia or symptoms of acid reflux with no changes on endoscopy; and gastritis, duodenitis, peptic ulcer; and oesophagitis A/B after initial healing course of PPI. Exclude patients with Barrett’s, Grade C/D oesophagitis, oesophageal cancer, Zollinger Ellison, oesophageal stricture/ulceration, oesophageal or gastric varices in banding programme, gastric cancer, need for gastroprotection, under current secondary care follow up. See full guidance for more information.

Consider antacid/alginate after meals and at bedtime at all stages of the step up and down ladder

Omeprazole 20mg BD* or equivalent review in 1 month

Omeprazole 20mg or equivalent once daily for a further month

*unlicensed dose

Symptoms recur

Consider seeking specialist advice/alternative diagnosis or for proven non ulcer dyspepsia consider use of ranitidine instead of PPI

Omeprazole 40mg BD* or equivalent and no ongoing symptoms

This dose should only be used for patients with Grade A/B oesophagitis under specialist advice

Symptoms recur

Reduce to omeprazole 10mg daily or equivalent for one month / and then stop; and to return if symptoms return/new symptoms develop.

Patients with oesophagitis A/B with one failed attempt at stopping PPI should thereafter be maintained on the lowest effective dose of PPI

Symptoms controlled

Symptoms recur

Patient on omeprazole 40mg BD* or equivalent and no ongoing symptoms

This dose should only be used for patients with Grade A/B oesophagitis under specialist advice

Symptoms recur

Seek specialist advice/alternative diagnosis.

Symptoms recur

Omeprazole 20mg BD* or equivalent and no ongoing symptoms

This dose should only be used for patients with Grade A/B oesophagitis under specialist advice

Symptoms recur

Seek specialist advice/alternative diagnosis.

Symptoms recur

Omeprazole 20mg BD* or equivalent and no ongoing symptoms

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Symptoms recur

Seek specialist advice/alternative diagnosis.
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