PPIs are very effective and well-tolerated drugs for dyspeptic symptoms resulting from gastro-oesophageal reflux disease (GORD) or peptic ulcer disease. Most guidelines for the management of GORD\textsuperscript{1–5} recommend:
- an initial 4–8 week course of standard-dose PPI for moderate to severe GORD to rapidly control symptoms and heal oesophagitis, \textit{then}
- \textit{‘step-down’ to the minimum PPI dose} that maintains symptom control following initial course. Step-down options include low dose PPIs and intermittent, symptom-driven therapy.

NOTES:
The number of PBS prescriptions dispensed for PPIs has doubled in the 2 years since PBS authority listing was removed in 2001.
Since over 90\% of all PPI prescriptions are for higher strength products\textsuperscript{6}, it appears there are some patients in whom a trial of a lower maintenance dose could be considered.
\textsuperscript{a} Lower strength products: esomeprazole 20 mg, lansoprazole 15 mg, omeprazole 10 mg, pantoprazole 20 mg, rabeprazole 10 mg.
\textsuperscript{b} Higher strength products: esomeprazole 40 mg, lansoprazole 30 mg, omeprazole 20 mg, pantoprazole 40 mg, rabeprazole 20 mg.

Establish whether ongoing PPI therapy is necessary for each patient
The goal of initial therapy may have been to:
- aid diagnosis of GORD
- relieve reflux-induced or dyspepsia symptoms
- heal oesophagitis
- heal peptic ulcers
- prevent NSAID or other drug-induced peptic ulcers or symptoms.\textsuperscript{1}
Following the initial therapy, review the success of treatment for each patient with a view to reducing or ceasing PPIs as appropriate.\textsuperscript{1,4}

Tips for when to review PPI therapy
- \textbf{✓} \textit{After 4 weeks} initial therapy at standard-dose for \textit{GORD, ulcer healing or oesophagitis}.\textsuperscript{1,2}
- \textbf{✓} \textit{After 8 weeks} \textit{where} initial therapy was continued for a further 4 weeks for \textit{GORD, ulcer healing or oesophagitis}.\textsuperscript{1,2}
- \textbf{✓} For patients whose PPI was \textit{initiated during hospitalisation} where there is not a clear indication.
- \textbf{✓} Regularly \textit{where co-prescribed medications may induce reflux/dyspepsia symptoms}.
- \textbf{✓} \textit{Whenever} repeat prescriptions are requested.
### Comparative information for proton pump inhibitors

<table>
<thead>
<tr>
<th>Indications</th>
<th>Omeprazole (Acimax, Losec, Probrin tablet, capsule)</th>
<th>Lansoprazole (Zotan) capsule, granules (for suspension)</th>
<th>Pantoprazole (Somac) tablet</th>
<th>Rabeprozole (Pariet) tablet</th>
<th>Esomeprazole (Nexium) tablet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peptic ulcer</td>
<td>initially 20–40 mg/day then 20 mg/day</td>
<td>initially 30 mg/day then 15–30 mg/day</td>
<td>initially 40 mg/day</td>
<td>initially 20 mg/day</td>
<td></td>
</tr>
<tr>
<td>GORD</td>
<td>20 mg/day</td>
<td>30 mg/day</td>
<td>40 mg/day</td>
<td>20 mg twice/day</td>
<td>40 mg twice/day</td>
</tr>
<tr>
<td></td>
<td>20 mg twice/day</td>
<td>30 mg twice/day</td>
<td>40 mg twice/day</td>
<td>20 mg twice/day</td>
<td>40 mg twice/day</td>
</tr>
<tr>
<td></td>
<td>reduce to minimum dose required</td>
<td>reduce to minimum dose required</td>
<td>reduce to minimum dose</td>
<td>reduce to minimum dose</td>
<td>reduce to minimum dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>required*</td>
</tr>
<tr>
<td>Scleroderma oesophagus</td>
<td>seek specialist advice</td>
<td>seek specialist advice</td>
<td>seek specialist advice</td>
<td>seek specialist advice</td>
<td>seek specialist advice</td>
</tr>
<tr>
<td>Zollinger-Ellison (Z-E) syndrome</td>
<td>up to 120 mg/day</td>
<td>up to 180 mg/day</td>
<td>up to 240 mg/day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment and prophylaxis of ulcers and erosion associated with NSAID use</td>
<td>treatment: 20–40 mg/day 4–8 weeks prophylaxis: 20 mg/day</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H. pylori eradication (in combination with dual antibiotic therapy for 1 week)</td>
<td>20 mg twice/day</td>
<td>30 mg twice/day</td>
<td>40 mg twice/day</td>
<td>20 mg twice/day</td>
<td>20 mg twice/day</td>
</tr>
<tr>
<td>Higher strength products</td>
<td>20 mg</td>
<td>30 mg</td>
<td>40 mg</td>
<td>20 mg</td>
<td>40 mg</td>
</tr>
<tr>
<td>Lower strength products</td>
<td>10 mg</td>
<td>15 mg</td>
<td>20 mg</td>
<td>10 mg</td>
<td>20 mg*</td>
</tr>
</tbody>
</table>

- PBS: Not an approved indication but an accepted indication due to evidence available for their efficacy.
- PBS Restricted Benefit (as at May 2004).
- PBS: Prescribing PPI for indications other than restricted benefits on the PBS should be by private prescription.

#### Key:
- ✓: Indicated for use
- ✗: Not indicated

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### All PPIs are very effective in controlling GORD symptoms and are clinically equivalent in most patients

Most clinical studies show that all PPIs have similar efficacy in the treatment of acid-related gastrointestinal disorders. Some studies have shown small differences but these studies have not always used equivalent doses.

- Healing rates at 8 weeks in erosive oesophagitis for example are in excess of 80%:
  - omeprazole 20 mg vs esomeprazole 20 mg (87% vs 90%)[^1]
  - lanosprazole 30 mg vs esomeprazole 40 mg (89% vs 93%)[^2]
  - omeprazole 20 mg vs esomeprazole 40 mg (84% vs 94%), or 87% vs 94%[^3]

- Maintaining remission in healed erosive oesophagitis ranges from 74% to 83% after 6 months maintenance treatment with lanosprazole 15 mg or esomeprazole 20 mg daily.[^4]

Efficacy and adverse effects may vary between patients. Failure of therapy or an adverse effect with one PPI should not preclude a trial with another.

### Adverse effects

- All PPIs have a similar adverse effect profile and no contra-indications for most users.
- Common adverse effects (incidence ≥ 1%): headache, nausea, diarrhoea, abdominal pain, dizziness and fatigue.
- Although individual risk of a serious adverse effect to a PPI is low, the high prevalence of use may lead to a higher burden of adverse effects.

### Interactions


### Hepatic/renal impairment: No dosage adjustment necessary for renal or mild/moderate hepatic impairment. Reduce PPI to the lowest dose possible in severe hepatic impairment.

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### Decrease PPI use to low doses or intermittent, symptom-driven therapy once GORD symptoms are controlled

#### Step-down options

- **Low-dose PPIs:** 70–80% patients with GORD can control their symptoms on low doses of PPIs e.g. omeprazole 10 mg or equivalent.[^7]

- **Interruption, symptom-driven use:** patients with GORD take a PPI on days when symptoms occur e.g. omeprazole 10–20 mg or equivalent 2–3 days per week.

- **Ceasing PPIs:** a trial of withdrawal of PPI is recommended after the initial successful treatment course. Many people with milder disease can manage symptoms with lifestyle changes, antacids and H2-antagonists if needed.[^8] If transient rebound hypersecretion occurs following cessation, consider H2-antagonists or antacids to reduce discomfort.

Ceasing PPI is not appropriate in patients with severe oesophagitis or other complications such as strictures, scleroderma, Zollinger–Ellison syndrome or Barrett’s oesophagus.[^9] These patients will require ongoing full or double-dose PPI therapy.[^10] However, regular review for efficacy, drug interactions and adverse effects is recommended.

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For more detailed information about the above drugs, refer to the Australian Medicines Handbook 2004 and the approved product information for the drug. Further information can be obtained from TAIS on 1300 138 677.

[^1]: No dosage adjustment necessary for renal or mild/moderate hepatic impairment. Reduce PPI to the lowest dose possible in severe hepatic impairment.

[^2]: The lowest available tablet strength of esomeprazole in Australia is 20 mg. Clinical trials have not always used equivalent doses when comparing PPIs.

[^3]: Source: This table is based on materials developed by the Drug and Therapeutics Information Service (DTIS), and information from references 2, 3, 7, and 8.

[^4]: Further information can be obtained from TAIS on 1300 138 677.
Consider testing for and treating *Helicobacter pylori* in people with uninvestigated dyspepsia or who are using PPIs long term

Test for *H. pylori* in people

- with uninvestigated dyspepsia.
  - "Test and treat" approach may improve symptoms and reduce rates of referral for endoscopy more than empiric PPI therapy.1,10
  - Refer candidates who are over 45–50 years of age and present with uninvestigated, persistent dyspepsia (GORD excluded), or with ALARM symptoms for endoscopy and specialist management.1
- on long-term PPIs (e.g. 12 months or more). This approach may reduce the risk that long-term acid suppression in the presence of *H. pylori* may lead to atrophic gastritis and ultimately gastric cancer.1,11

Those whose *H. pylori* test is:

- **positive** should receive eradication therapy (Klacid Hp7, Losec Hp7 or Nexium Hp7)
- **negative** and who have uninvestigated dyspepsia may benefit from a short course of a PPI.4

Test in candidates who meet all of the following:
- Aged < 45–50 years
- Dyspepsia lasting > 4 weeks
- Dyspepsia not previously investigated
- No ALARM symptoms
- Not an NSAID user
- GORD has been excluded

<table>
<thead>
<tr>
<th>H. pylori tests</th>
<th>When to use and limitations</th>
<th>13C/14C–Urea Breath Test (C-UBT)</th>
<th>Faecal Antigen Test (PAT)</th>
<th>Serology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use to detect presence of <em>H. pylori</em></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Use to confirm eradication of <em>H. pylori</em> a minimum of 4 weeks after eradication therapy</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Interference by PPI (withhold for 2 weeks prior to test)</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Interference by antibiotics (withhold for 4 weeks prior to test)</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>

ALARM (or ALARMS) symptoms1

A – Anaemia
L – Loss of weight
A – Anorexia, early satiety
R – Recurrent symptoms or previous gastric ulcer or gastric surgery
M – Mass/Melaena
S – Swallowing difficulties, recurrent vomiting or vomiting up blood

**Encourage lifestyle modifications in all patients**

Suggest lifestyle changes for patients with:
- mild, occasional, reflux symptoms who can be managed with ‘as required’ use of antacids or *H₂* antagonists6
- significant reflux diseases an adjunct to appropriate drug therapy to help prevent breakthrough symptoms.

**Lifestyle changes**4,15:
- avoid risk factors such as smoking or excess alcohol
- avoid provoking factors such as caffeine, chocolate, fatty or spicy foods, eating just before going to bed, tight clothing, supine position and excess weight
- prop up the bedhead.

**Review use of medications that induce dyspepsia symptoms**

Identify drugs known to induce reflux4 and review ongoing need. Such drugs include NSAIDs and
- bisphosphonates e.g. alendronate
- tetracyclines e.g. doxycycline
- some calcium channel blockers e.g. amlodipine
- nitrates
- theophylline.

**Avoid NSAIDs where possible**

For people who require continued NSAID use and with several concomitant risk factors e.g. over 65 years, or those with a prior ulcer, prophylaxis should be considered.2 Options include high-dose *H₂* antagonists2, PPIs4,14 and/or substitution with a COX-2 selective NSAID.4 PPIs are not subsidised on the PBS for NSAID-induced ulcer prophylaxis. Omeprazole and pantoprazole only are approved for NSAID-induced ulcer prophylaxis in Australia currently.

**References**

14. www.clinicalevidence.com