



National Prescribing Service Limited

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Prescribing Practice Review

No. 45 Proton pump inhibitors: step-down to symptom control

Dear Dr Sample,

This issue of *Prescribing Practice Review* focuses on proton pump inhibitor (PPI) therapy in gastro-oesophageal reflux disease (GORD). Included are confidential data on your prescribing of PPIs, along with practical information for your review.

Although the volume of PPIs prescribed continues to rise, the rate of increase has slowed in recent years.¹ Evidence of rare but serious adverse effects highlights the need to continue to focus on using PPIs judiciously.

We outline the key step-down strategies, using low-dose PPI either continuously or on a symptom-driven basis, and when to consider a trial withdrawal. We discuss lifestyle recommendations that may help to reduce reliance on medication, and information for patients considering reduced PPI therapy.

The clinical audit *Review of proton pump inhibitor (PPI) prescribing* is available as an additional tool to help you review your prescribing. For further information please see the enclosed enrolment form, or enrol online at www.nps.org.au.

Yours sincerely

Dr Janette Randall
Chair, National Prescribing Service Limited

Reference

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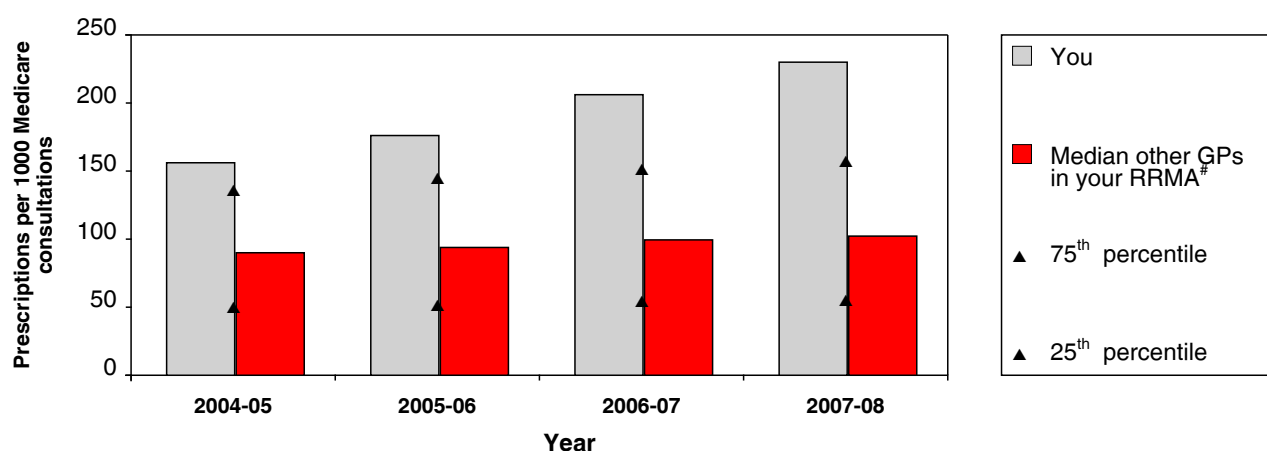
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Your confidential prescribing data

The data presented from Medicare Australia include PBS prescriptions for proton pump inhibitors (PPI) dispensed for your patients if the drug is above the general patient co-payment or, if the drug is below the general patient co-payment, it includes only those prescriptions dispensed for concession card holders i.e.:

- pantoprazole 20 mg from April 2005
- lansoprazole 15 mg from August 2005
- omeprazole 10 mg from January 2006 and
- rabeprazole 10 mg from January 2005 - December 2006.

Total proton pump inhibitor use



Proton pump inhibitor use by strength

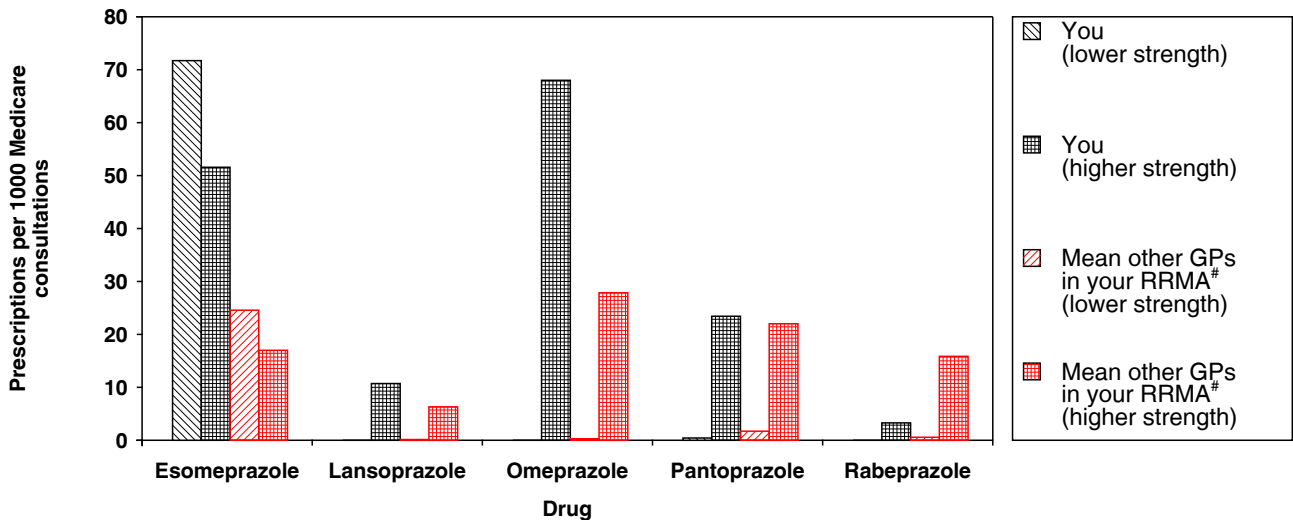
	You		Median other GPs in your RRMA [#]	
	Percentage of prescriptions		Percentage of prescriptions	
	2006-07	2007-08	2006-07	2007-08
Lower strength products esomeprazole (<i>Nexium</i>) 20 mg lansoprazole (<i>Zoton</i>) 15 mg omeprazole (<i>Losec</i>) 10 mg pantoprazole (<i>Somac</i>) 20 mg rabeprazole (<i>Pariet</i>) 10 mg	35%	31%	21%	23%
Higher strength products esomeprazole (<i>Nexium</i>) 40 mg lansoprazole (<i>Zoton</i>) 30 mg omeprazole (<i>Acimax</i> , <i>Meprazol</i> , <i>Losec</i> , <i>Omepral</i> , <i>Probitor</i>) 20 mg pantoprazole (<i>Somac</i>) 40 mg rabeprazole (<i>Pariet</i>) 20 mg	65%	69%	79%	77%

Percentages may not add up to 100 due to rounding of median values.

Practice points

- Use a step-down approach for maintenance therapy. Low dose PPI can control dyspepsia in 70-80% of patients with healed oesophagitis and many can have the therapy ceased.¹
- Has your prescribing of lower strength esomeprazole increased?

Use of higher versus lower strength products in 2007-08



Practice points

- Consider how you choose which PPI to use. The clinical efficacy is similar for all five PPIs and newer drugs offer no advantages in terms of clinical efficacy, long term safety or cost.^{2,3}
- Due to the prevalence of PPI use, although rare, serious adverse events with PPIs are a concern. Review the need for ongoing therapy in patients recently discharged from hospital or at the request for a repeat prescription.

	You		Median other GPs in your RRMA [#]	
	2006-07	2007-08	2006-07	2007-08
Number of patients (and percentage of those prescribed a PPI) who have had more than 6 PPI prescriptions dispensed	95 56%	94 59%	34 38%	37 38%

Practice points

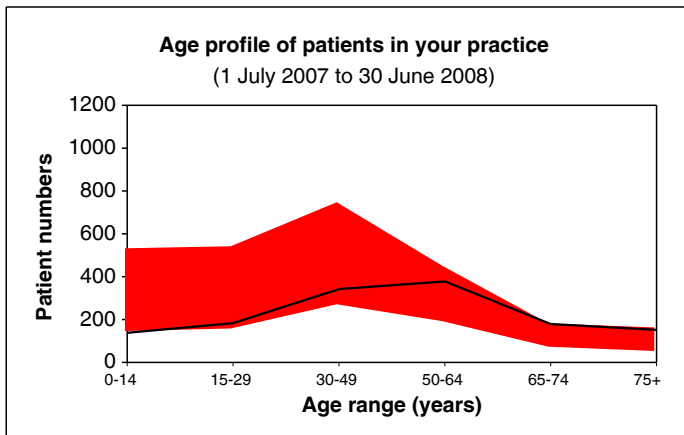
- Identify patients on long-term PPI therapy and review the need for continuing use.
- A single 4-week initial course of standard-dose PPI is usually appropriate in uninvestigated dyspepsia or newly diagnosed GORD; review patients with persistent or recurrent symptoms.⁴
- In 2007-08, **87%** of PPI prescriptions were for the maximum number of 5 repeats. Does your prescribing software default to the maximum number of repeats?

Number and cost of proton pump inhibitor prescriptions dispensed

Year	You			All GPs nationally		
	Number of prescriptions	Total cost \$	Percentage of your total PBS cost	Number of prescriptions	Total cost \$	Percentage of total PBS cost
2004-05	1,036	54,773	10%	9,978,417	502,920,760	10%
2005-06	1,134	57,123	10%	10,759,841	522,950,441	10%
2006-07	1,161	49,569	10%	11,500,652	483,639,163	9%
2007-08	1,117	48,316	10%	12,437,429	521,014,023	10%

Practice profile

Some data shown earlier are presented as prescribing rates (per 1000 Medicare consultations) to adjust for volume of service. Age profile and concession card holding status of patients in your practice are provided to assist you in interpreting your prescribing data.



The black line represents the age profile of patients in your practice. 25% to 75% of other GPs in your RRMA[#] fall within the shaded area.

Medicare patients and concession card holders in your practice
(1 April 2008 to 30 June 2008)

Patients	You	Median other GPs in your RRMA [†]
Total Medicare	783	691
Concession card holders^{##}	333	181

Data from a three month period (1 April 2008 to 30 June 2008) that best represent your patient mix have been provided.

Notes

[@] Data shown are an aggregate for all your provider locations

[#] The comparator group "other GPs in your RRMA" includes all prescribers who are currently located in a similar geographical region i.e. 1. capital cities, 2. other metropolitan centres, 3. large rural centres, 4. small rural centres, 5. other rural centres, 6. remote centres and 7. other remote centres.

Your RRMA peer group is **1**.

[▲] 25% to 75% of "other GPs in your RRMA" fall in the range shown by the triangular symbols.

^{##} Includes those reaching Safety Net.

Confidentiality

NPS has a contract with Medicare Australia to provide your prescribing feedback data directly to you. NPS does not have access to these data. The data contained in this feedback are not used for any regulatory purposes.

Discrepancies may occur between the data provided and your own prescribing practice. This may be due to either inaccurate recording of your prescriber number in the pharmacy or your prescription pad having been used by another doctor.

If you consider your individual data to be incorrect, have other data queries or general feedback, please contact NPS on 02 8217 8700 or by email at info@nps.org.au

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Proton pump inhibitors: step-down to symptom control

KEY MESSAGES

- Use a 4–8 week course of standard-dose PPI therapy to control symptoms of GORD
- Communicate to patients that adopting lifestyle changes can help reduce the need for PPI therapy
- Step-down to the lowest dose and frequency of PPI that is effective
- Review the need for ongoing maintenance therapy as rare, but serious, PPI side effects can occur

PPIs are widely held to be safe medicines. However, evidence of potentially serious adverse effects merits consideration. By stopping therapy when appropriate — or using PPIs for the shortest time and at the lowest effective dose — the benefit can be preserved and the risk of serious adverse effects reduced.

Starting proton pump inhibitor therapy

Confirm symptoms, refer if necessary

Proton pump inhibitors (PPIs) effectively control heartburn, but many people have a poor understanding of this term. Provide a clear description such as “a burning feeling rising up from your stomach or lower chest towards the neck”.¹

Refer patients for endoscopy if alarm symptoms (anaemia, difficulty or pain on swallowing, evidence of gastrointestinal bleeding, weight loss or vomiting) are present.^{1,2}

Review medicines

Ask patients to bring a list of all their medicines to each visit.³ Discontinue or reduce the dose of any medicine that could contribute to symptoms (e.g. calcium channel blockers, nitrates, NSAIDs, theophylline⁴) where appropriate.

4–8 weeks of PPI therapy relieves symptoms and heals oesophagitis

Prescribe an initial 4-week course of standard-dose PPI (see Table 1) after excluding alarm symptoms. Initial standard-dose therapy heals oesophagitis in more than 70% of patients.⁵

Review patients after the initial 4-week course. Manually setting electronically-generated prescriptions to the minimum quantity needed can be a trigger for patients to return for review.⁶

An additional 4-week course of standard-dose therapy is appropriate in patients with persistent symptoms. Oesophagitis healing rates are increased by a further 14% if therapy is extended to 8 weeks.⁵ Refer patients for endoscopy if response is inadequate after 8 weeks.²

Many patients will not need continuous, long-term PPI therapy

Consider a trial cessation or reduced therapy if initial treatment is successful.¹

Always review the need for ongoing PPI therapy following hospital discharge. Stop the PPI when the initial indication no longer exists and when there is no need for further therapy.

PPI maintenance therapy is not usually necessary after successful eradication of *Helicobacter pylori* ulcers.²

Over-the-counter PPI therapy

PPI therapy does not always require a prescription

Pantoprazole 20 mg (Somac Heartburn Relief) is available over the counter (pharmacist only medicine) for symptomatic relief of heartburn, acid regurgitation and other symptoms associated with GORD.⁷

Pharmacists should ask about symptoms and patient history

Pharmacists should establish whether patients requesting over-the-counter pantoprazole need PPI therapy, provide lifestyle advice and describe treatment options.

Confirm that symptoms occur on two or more days a week. Refer to a doctor for further investigation when:

- alarm symptoms are present, or symptoms are non-specific or atypical
- symptoms occur daily
- the individual is 55 years or older with first-time or long-standing, frequent and troublesome symptoms
- symptoms are not controlled after two weeks of continuous over-the-counter pantoprazole 20 mg
- there is a family history of gastrointestinal cancer, or the individual is receiving long-term NSAID therapy.⁸

Refer to the Pharmaceutical Society of Australia protocol — Provision of pantoprazole as a pharmacist only medicine — for further guidance.⁸

Suggest lifestyle changes

Discuss diet and weight loss

A written record of episodes of reflux and the foods consumed beforehand may help patients to identify specific triggers.

Encourage weight loss in overweight patients. Being overweight or obese is associated with a 1.4- or 1.9- fold greater risk of symptoms of GORD, respectively, compared with normal-weight people.⁹

Target behaviours that contribute to or reduce reflux

Quitting smoking and moderating alcohol consumption should be part of the management plan. Cigarette smoking and alcohol consumption (≥ 7 standard alcoholic drinks per week) are risk factors for GORD.¹⁰

Patients experiencing night-time symptoms may benefit from elevating the head of their bed.¹¹

Table 1. Dose comparison of prescription only proton pump inhibitors

PPI	Standard dose*	Low dose*
esomeprazole (Nexium)	20 mg daily [†]	20 mg daily
lansoprazole (Zoton)	30 mg daily	15 mg daily
omeprazole (Acimax, Losec, Meprazol, Omepral, Probitor)	20 mg daily	10 mg daily
pantoprazole (Somac)	40 mg daily	20 mg daily
rabeprazole (Pariet)	20 mg daily	10 mg daily

* Standard dose refers to the initial therapeutic trial dose that should be used to provide symptom relief and heal erosive disease.² Low dose refers to the lower dose recommended for maintenance therapy for gastro-oesophageal reflux disease.³

[†] Esomeprazole 20 mg is recommended as the initial therapeutic trial dose to provide symptom relief and heal erosive disease.² Esomeprazole 40 mg daily is a PBS-listed restricted benefit for healing of gastro-oesophageal reflux disease, and may be appropriate if there is endoscopically proven erosive disease in a previously untreated patient.²

Trial a withdrawal and use step-down strategies

Assess management options at patient review

Determine whether ongoing therapy is required when patients attend for review or request a repeat prescription. Consider reduced PPI therapy in all patients **except** those with: severe oesophagitis, oesophageal stricture or scleroderma; Barrett's oesophagus; or Zollinger–Ellison syndrome.

Manage patients with severe disease in consultation with a gastroenterologist.² Patients with severe oesophagitis should be treated with ongoing, standard-dose PPI; complications such as strictures will require endoscopic therapy.¹

What to tell patients about reduced PPI therapy

Patients whose symptoms are well controlled by PPIs may be reluctant to reduce the dose or frequency of their medication. Emphasise that reduced PPI therapy can maintain symptom relief and that:

- symptom-driven therapy will mean taking fewer tablets
- prescription costs may be lower
- there is less risk of unwanted side effects when less medicine is used.

Patient information leaflets — one that allows GPs to detail individual step-down approaches, and the other about PPI use and self-management strategies — are available at: www.nps.org.au/patient_leaflets

Consider a trial withdrawal if initial PPI therapy is successful

Between 20% and 40% of patients may not require PPI therapy for up to 1 year after successful treatment of GORD.⁵ In one small trial, 21% of long-term PPI users previously treated for GORD did not use PPIs during a 1 year follow-up.¹² The comparable figure for patients with dyspepsia or other indications was 48%. Symptom-driven use of PPIs is appropriate if symptoms recur.¹

Asymptomatic patients maintained on long-term, standard-dose PPI may prefer to step-down to continuous or symptom-driven, low-dose therapy before a trial withdrawal.

Use continuous or symptom-driven low-dose PPI if maintenance therapy is required

Continuous, low-dose maintenance therapy prevents relapse in many patients with healed oesophagitis.^{5,13} About 55% of patients with reflux disease remained free of significant symptoms in clinical trials of 6 months to 1 year in duration.¹³

Alternatively, advise patients to take low-dose PPI when troublesome symptoms occur, and to continue until symptoms resolve. Survey data suggest that many patients use PPIs at their discretion, regardless of prescribed instructions.^{14,15} In randomised trials of patients with mild to moderate GORD or non-erosive reflux disease, symptom relief and patient satisfaction with low-dose, symptom-driven therapy was similar to that of continuous low-dose therapy.^{16,17}

Evidence for serious adverse effects

PPI therapy may be associated with harms

PPIs are generally considered to be safe, but evidence suggests an association between their use and serious adverse effects. These adverse effects may be rare and difficult to predict. PPIs should be prescribed judiciously, for the shortest possible time and at the lowest effective dose, to minimise risk.

PPIs increase the risk of *Clostridium difficile* infection

PPI use is a risk factor for *C. difficile* infection, possibly because of the profound reduction in gastric acidity.

In observational studies, PPI therapy was associated with about a 2–3 fold increased risk of *C. difficile* infection in hospital and community settings.^{18–20}

In a case-control study of community-acquired *C. difficile* infection, antibiotic- and PPI-use were the most important medication-related risk factors.²¹

Acute interstitial nephritis and PPIs

Data collected from 2 Australian teaching hospitals over a 10-year period showed that 18 of 28 cases of biopsy-proven acute interstitial nephritis were associated with PPI use.²²

The symptoms of acute interstitial nephritis are non-specific; those reported include weight loss, fatigue, malaise, nausea and vomiting.^{22,23} A dose–response relationship has not been established and onset may be delayed.²³ Assess renal function by serum creatinine if renal impairment is suspected; withdraw PPI and refer to a nephrologist if confirmed.

Evidence for other possible serious adverse effects

Several studies have suggested that PPIs may reduce the efficacy of clopidogrel, although the evidence is not consistent.²⁴⁻²⁸ The US Food and Drug Administration has advised that patients currently taking clopidogrel should continue to do so, while the need for starting or ongoing PPI therapy should be reviewed.²⁹ Studies are underway to further investigate this potential interaction.

Case-control studies report a modest, but significant, association between long-term PPI use and hip fracture.^{30,31} Risk of hip fracture increased

with duration of therapy^{30,31}, and when patients took high doses of PPI for more than 1 year.³⁰ In Australia, the Adverse Drug Reactions Advisory Committee (ADRAC) has received two reports of pathological fracture and/or osteoporosis associated with PPI use.³²

Evidence from large case-control studies suggests an association between current PPI use and community-acquired pneumonia.³³⁻³⁵ The risk was greatest in patients who started treatment within the previous 7 days.^{33,34} Those with a longer history of PPI use had a modest, or no, increased risk.

Expert reviewer

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The information contained in this material is derived from a critical analysis of a wide range of authoritative evidence. Any treatment decisions based on this information should be made in the context of the clinical circumstances of each patient.



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