NPS MEDICINEWISE

MEDICINEWISE NEWS
June 2018

StePPIng the appropriate path with GORD medicines

GORD is a frequently managed condition

Gastro-oesophageal reflux disease, or GORD, is a commonly managed condition in primary care. In 2015–16, GORD accounted for 13.2% of all new problems managed in general practice in Australia, and was ranked eighth behind hypertension, upper respiratory tract infection, depression, diabetes, arthritis, back complaints and lipid disorders.[1]

People can be diagnosed with GORD if they have two or more reflux episodes per week, or if they have symptoms severe enough to significantly impair their quality of life.[2]

Heartburn – a symptom of GORD – is experienced by 15% to 20% of adults at least once each week.[2,3]

PPIs are frequently prescribed medicines

Proton pump inhibitors (PPIs) are among the most commonly prescribed medicines in Australia.[4]

They are effective for the treatment of GORD, but they are sometimes being used inappropriately.[2]

Statistics from the Pharmaceutical Benefits Scheme (PBS) for prescriptions in 2016–17 show:[a,4]

- two of the five available PPIs rank in the top five medicines by prescription volume[b]
- four of the five available PPIs are among the top 30 medicines by prescription volume[b]
- PPIs accounted for 16% of all top 30 medicines by prescription volume.

Data from the Bettering the Evaluation and Care of Health (BEACH) program illustrate the frequency of PPI use among general practice patients in Australia, and the conditions for which they were prescribed.[5]

From 1998–2017, BEACH collected data from approximately 1,000 randomly sampled GPs across Australia every year. The project has a database of over 1.7 million GP–patient encounters.[6]

Based on data acquired from 2,642 general practice patients enrolled in BEACH in 2015–16, 17.9% of patients were currently taking a PPI (14.2%) or had taken one in the past 12 months (3.7%).[5] Within this subgroup, most were doing so for oesophageal reflux (67.9%).[5]

[a] Data are for prescriptions made under the PBS General Schedule (including doctor's bag and under-copayment prescriptions).

[b] Among the top 50 medicines sorted by highest total prescription volume in 2016–17 (including doctor's bag and under-copayment prescriptions), the PPIs rank: 3. esomeprazole, 4. pantoprazole, 25. rabeprazole, and 30. omeprazole. (Atorvastatin and rosuvastatin were ranked 1 and 2 respectively.)

Using PPIs for GORD wisely

The appropriate use of PPIs depends on:[2]

1. only starting treatment with a PPI for 4 to 8 weeks with patients who have been diagnosed with GORD (according to the definition above)
2. regularly reviewing patients who are taking PPIs for the treatment of GORD, with the aim of reducing or stopping PPI treatment if symptoms are well controlled.

These approaches align with Choosing Wisely Australia's recommendations from the Royal Australian College of General Practitioners (RACGP) and the Gastroenterological Society of Australia (GESA) on the appropriate use of PPIs in clinical practice.[7,8]

- RACGP Choosing Wisely recommendation 1: Don't use PPIs long term in patients with uncomplicated disease without regular attempts at reducing dose or ceasing.
- GESA Choosing Wisely recommendation 3: Do not continue prescribing long-term PPI medication to patients without attempting to reduce the medication down to the lowest effective dose or cease the therapy altogether.

There is evidence that approaches similar to these can reduce PPI use – from the initiative known as 'Bye-Bye, PPI'.[9]

Bye-Bye, PPI

The 'Bye-Bye, PPI' program is a joint initiative between Choosing Wisely Canada and the Toronto Western Hospital Family Health Team.[9]

It was inspired by the observation that PPIs are often used inappropriately, without an indication, or for longer durations than recommended.[9]

The program aligns with one of Choosing Wisely Canada's recommendations from the Canadian Association of Gastroenterology.[9,10]

Don't maintain long-term PPI therapy for gastrointestinal symptoms without an attempt to stop/reduce PPI at least once per year in most patients.[10]

Electronic medical record (EMR) messaging reminded primary care providers to reassess treatment for adults who had been taking a PPI for 8 weeks at an upcoming periodic health examination.[9]

A prescribing toolkit was uploaded to the EMR system as a standardised guide for the reassessment of PPI treatment where indicated.[9]

As a result of this strategy, 43 patients, of 46 patients taking a PPI, had their PPI reassessed (93%), and PPIs were deprescribed for 11 patients (26%).[9,11]

Of the 11 patients for whom a PPI was deprescribed, six stopped taking a PPI, four were taking an alternative medicine, and one attempted to taper their PPI dose but resumed the original dose because they experienced worsening gastrointestinal symptoms.[11]

Is it GORD?

When a person presents with reflux symptoms, health professionals must distinguish between what is GORD and what is not GORD before prescribing a PPI.

As part of the patient assessment and diagnosis, possible causes of reflux and factors that can exacerbate it should be explored.[2,3]

A person is likely to have GORD if they have reflux symptoms that are

- *frequent – two or more episodes per week or*
- *severe enough to significantly impair their quality of life.*[2]

View the algorithm developed by NPS MedicineWise

People with GORD may experience typical reflux symptoms, such as heartburn, regurgitation or waterbrash (sudden and brisk stimulation of salivation).[3] They may also experience atypical symptoms that are non-specific and not easily recognised as being due to reflux.[3]

These atypical symptoms may include chest pain, throat or voice changes, coughing, asthma, excessive belching, dyspepsia and nausea.[3]

The symptoms of GORD may be directly related to reflux episodes (such as heartburn and regurgitation) or due to complications of reflux disease (such as difficult or painful swallowing).[3]

For patients who have typical reflux symptoms and no alarm symptoms, response to a trial of PPI therapy can confirm the diagnosis of GORD.[2]

When is it gastro-oesophageal reflux, but not GORD?

Gastro-oesophageal reflux is a normal physiological event that usually occurs after eating, but GORD occurs when exposure of the oesophagus to the gastric contents becomes excessive.[2,3]

Symptoms of gastro-oesophageal reflux – in contrast to gastro-oesophageal reflux disease – are mild and intermittent, and do not significantly impair wellbeing or quality of life.[2,3]

If people have gastro-oesophageal reflux, their symptoms occur no more than once per week and are usually related to what they eat or drink.[2]

Are there any red flags that require further investigation of upper GI symptoms?

Endoscopy is NOT routinely recommended for patients with typical reflux symptoms.[2]

However, health professionals are advised to refer patients for endoscopy if any of the following red flags are present:[2,12]

- difficulty swallowing (dysphagia)
- painful swallowing (odynophagia)
- unexplained weight loss
- persistent vomiting
- blood in vomit (haematemesis) or dark black, tarry, sticky faeces (melaena)
- signs or symptoms of anaemia
- new onset of persistent symptoms in those over 55 years of age.

Are there any underlying causes of reflux symptoms?

Gastro-oesophageal reflux symptoms are commonly induced by dietary triggers which may include high-fat meals, alcohol, coffee, chocolate, citrus fruit, tomato products, spicy foods, carbonated beverages and smoking.[2,3]

Some medicines may also cause or contribute to reflux symptoms, including:[12,13]

- aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs)
- benzodiazepines
- bisphosphonates
- calcium channel blockers
- medicines with anticholinergic effects, such as tricyclic antidepressants
- nitrates.

Should GORD patients be tested for *H pylori* infection?

Symptoms of GORD can overlap with the gastrointestinal symptoms caused by *Helicobacter pylori* (*H pylori*) infection.[2] The prevalence of *H pylori* infection is higher in people who are older, migrants, of lower socioeconomic status or institutionalised. The likelihood of *H pylori* infection is related most strongly to living conditions in childhood (when acquisition usually occurs).[2]

Patients with reflux-predominant symptoms are usually treated with acid-suppression therapy. Non-invasive testing and treating for *H pylori* (the 'test-and-treat' strategy) is a cost-effective strategy for younger adult patients (generally under 50 years, but younger if the patient is from a higher risk country) with dyspepsia and no red flags. Some guideline bodies recommend testing for *H pylori* before starting long-term PPI therapy for GORD.[2]

The usual choice of diagnostic test is the C13- or C14-urea breath test. The C13-urea breath test is not radioactive and is preferred for women of childbearing age. Before a breath test, antibiotic therapy should not be taken for at least 4 weeks, and PPI therapy should be withheld for at least 1 week (and preferably 2 weeks), to minimise the chance of false-negative results.[2]

The triple-therapy combining a PPI with amoxicillin and clarithromycin is the preferred first-line eradication treatment.[2]

Current Australian Therapeutic Guidelines for gastroenterology recommend *H pylori* eradication treatment in the following situations:[2]

- peptic ulcer disease (past or present)
- dyspepsia
- selected users of NSAIDs (including aspirin)
- atrophic gastritis and intestinal metaplasia
- patients requiring long-term acid suppression
- close relatives of patients with gastric cancer
- patients already treated for early gastric cancer
- low-grade gastric MALT lymphoma
- patient preference to be treated (after possible harms and benefits have been discussed)
- gastric cancer prevention in communities with high incidence of gastric cancer.

If tested, eradication therapy should be offered to patients found to be infected with *H pylori*.[2]

Starting a PPI for GORD

Diet and lifestyle modifications may be all that is required for people with mild intermittent reflux symptoms, but people with GORD will also need initial treatment with a PPI.[2]

For the initial treatment of GORD, PPIs are generally recommended over H_2 receptor antagonists because they are more effective at standard doses.[2]

A PPI is recommended at the standard dose (see Table 1), orally, once daily, 30 minutes to 1 hour before a meal.[2]

The initial course of PPI treatment should be for 4 to 8 weeks, following by a review. Treatment should be stepped down if symptom control is adequate after this initial course of treatment.[2] Higher doses of PPIs are not indicated for initial PPI treatment for GORD, and are rarely needed in most cases of GORD.[2]

All PPIs are thought to have similar efficacy and adverse effects, although they may differ in their potential to cause drug interactions.[14]

When it is gastro-oesophageal reflux, but not GORD

On-demand medicines may be used if diet and lifestyle changes alone cannot sufficiently control mild intermittent gastro-oesophageal reflux symptoms.[2]

In these situations, if as-required antacids (with or without alginates) do not provide adequate relief, then a PPI or an H_2 receptor antagonist can be considered alongside continued diet and lifestyle changes.[2]

A PPI is recommended at the standard dose, orally, 30 minutes to 1 hour before a meal, once daily as required.[2]

TABLE 1 **DOSAGE OF PPIs APPROVED FOR USE IN AUSTRALIA**[2,14,15]

PPI	STANDARD DOSE	LOW DOSE
Esomeprazole[c]	20 mg once daily	Not PBS listed
Lansoprazole	30 mg once daily	15 mg once daily
Omeprazole	20 mg once daily	10 mg once daily
Pantoprazole	40 mg once daily	20 mg once daily
Rabeprazole	20 mg once daily	10 mg once daily

[c] Esomeprazole 40 mg is not a standard dose. The lowest PBS-listed dose of esomeprazole is 20 mg; other low-dose preparations are appropriate step-down options for patients on esomeprazole 20 mg.

Which lifestyle changes are effective?

Overall, lifestyle changes represent no risk to patients, may contribute to reduced reflux symptoms, and can lead to improved health in general.

Stopping smoking

Data from epidemiological studies suggest that smoking is a risk factor for GORD.[16]

In the large population-based 'HUNT' study, stopping or reducing smoking led to an almost two-fold improvement in severe symptoms in people with normal BMI taking at least weekly antireflux medication, compared with those who continued to smoke.[17]

Losing weight

Australian GORD guidelines state that even modest weight loss can be effective for improving reflux symptoms in patients who are overweight.[2]

There is likely to be a dose-response relationship between increasing BMI and frequency of reflux symptoms.[16,18–20]

Changing diet

Anecdotal and experimental evidence varies about reflux symptoms and diet and alcohol use.[16]

Nonetheless, guidelines recommend that patients should try to identify and avoid their individual triggers while avoiding overly restricting their diet or persisting with measures that are not improving symptoms.[2,3]

Raising bedhead

If symptoms are worse at night or disrupt sleep, raising the head of the bed can reduce the number of reflux episodes, decrease reflux length and severity, or lead to faster acid clearance times.[16,21,22]

This can be achieved by placing 20 cm blocks under the head of the bed, or sleeping on a wedge pillow.[16]

Other changes

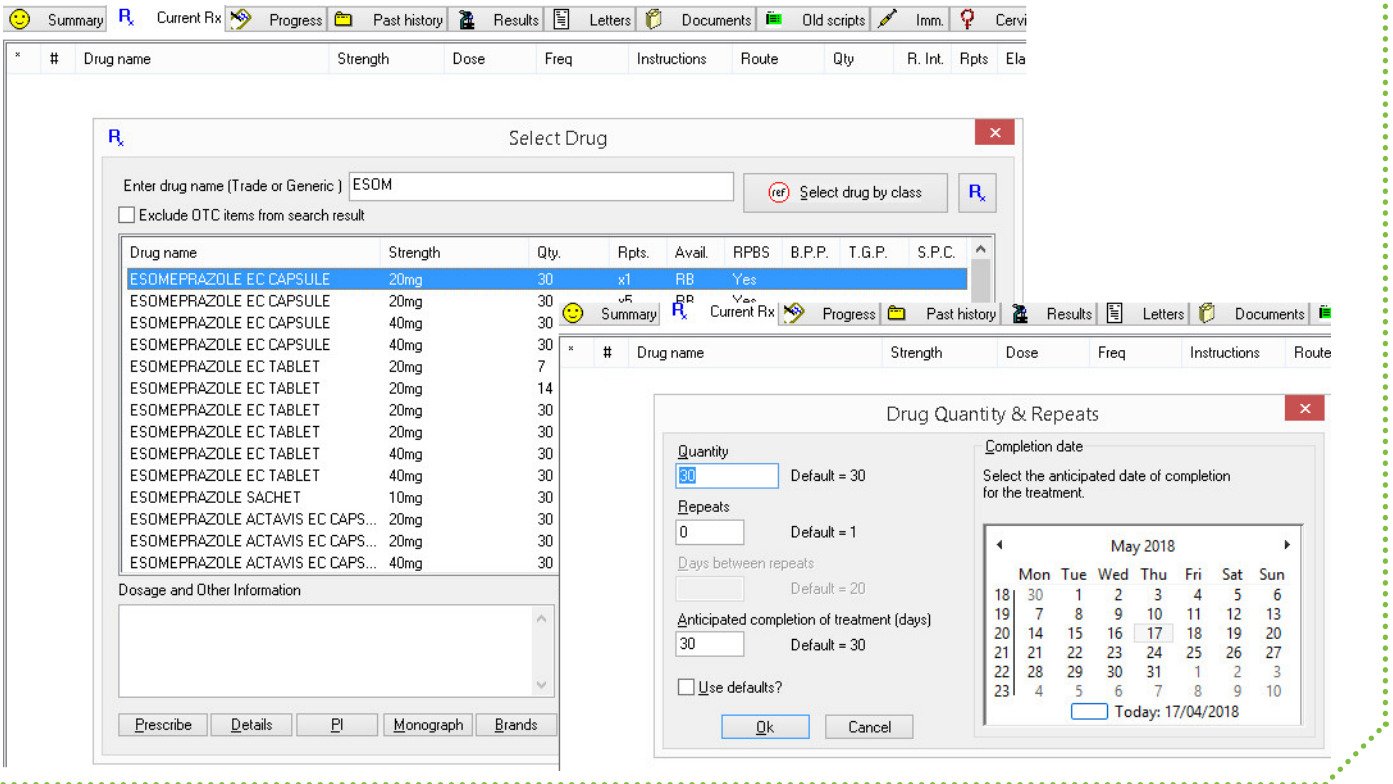
Reducing meal sizes, avoiding meals before bedtime, and avoiding vigorous exercise after eating may also help to reduce symptoms in some patients.[2,16]

How many PPI script repeats should be prescribed?

Australian guidelines recommend that a patient with GORD should be initially treated with a PPI for 4 to 8 weeks, then undergo a review.[2] This is equivalent to one or two prescription repeats.

In clinical information software, a GP can select a default to specify the duration of prescribed medication. Alternatively, the GP can change the number of repeats for each individual prescription. An illustration of how to do this in MedicalDirector is shown in Figure 1 below.

Figure 1. Selecting (top left) and setting (bottom right) 1–2 PPI scripts in MedicalDirector



Additional note for PPI prescribers in primary care

You may need to check whether a patient has come home from hospital with an inappropriate PPI prescription. Sometimes a patient is discharged with a PPI prescription without a valid indication. In some cases, these inappropriate PPI prescriptions may be continued in primary care, without apparent reason.[23] If there is no duration or end date for the prescription, checking the discharge summary may help.

Stepping down a PPI for GORD

If symptoms are controlled after an initial 4–8-week trial of a PPI, guidelines recommend that treatment is titrated down to the lowest dose and frequency that controls symptoms, or stopped.[2]

There are different options for 'stepping down' PPIs, and the approach should be individualised in consultation with the patient.

Patients can step down PPI medicines by

- taking the standard dose less often (for example, alternate-day dosing)
- reducing their PPI dose to a low dose
- or only taking PPIs 'on demand' when they experience symptoms.[2]

A patient may move between the different step-down options, depending on their level of symptom control.

If symptoms are well controlled, an attempt can be made to step down treatment further, or to stop. If symptoms return, the patient should step back up to the PPI dose that provided adequate symptom control.

*To see the different step-down options, view the algorithm developed by NPS MedicineWise as part of the **Starting, stepping down and stopping medicines** program.*

Clinical studies investigating strategies for PPI discontinuation have shown that PPIs can be discontinued without deteriorating symptom control in up to 64% of patients.[24] However, in the BEACH study mentioned above, just 23% of patients taking a PPI had attempted to reduce their dose in the last 12 months, and only 15% had attempted to stop.[5]

What if reflux symptoms are still not controlled?

If reflux symptom control is inadequate with a daily PPI, especially after treatment at the standard dose for at least 8 weeks, guidelines recommend that health professionals check with patients that they are taking their PPI regularly, and at the optimal time (30–60 minutes before meals).[2]

If adherence to therapy is confirmed, endoscopy is indicated to exclude other conditions.

Treatment with a PPI at a high dose may be considered if endoscopy supports a diagnosis of GORD.

For high-dose PPI treatment, guidelines note that a standard PPI dose given twice daily is more effective than a double dose given once daily.[2]

However, if symptoms still do not respond to PPI treatment, patients should be referred to a specialist for further investigation.[2]

Help your patients help themselves

As part of the *Starting, stepping down and stopping medicines* program, NPS MedicineWise has also developed a consumer-tested Patient Action Plan.

Patient Action Plan and fact sheet, Heartburn and reflux: Manage your medicine

Health professionals can print out the Patient Action Plan and use it with their patients to help explain the importance of using lifestyle changes together with PPIs to help manage symptoms.

Patients can identify their goals for stepping down and stopping their PPI medicines, and view a list of lifestyle changes that might help them manage their reflux symptoms.

Find the online version of this article at **nps.org.au/news/stepping-the-appropriate-path-with-gord-medicines**

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