# Optimising and reviewing Proton Pump Inhibitors (PPIs)

## Background information and adverse effects

PPIs are widely prescribed and the benefits of using them for treating several upper GI conditions and for gastroprotection are well known, with adverse effects such as headache, nausea and diarrhoea, usually being mild and reversible. However, there are concerns regarding the long-term risks of PPIs. Several observational studies have associated long-term use of PPIs with risks of several serious adverse effects.

NICE CKS information on proton pump inhibitors states that long-term treatment may be associated with uncommon, serious adverse effects such as *Clostridioides difficile* infections, increased risk of bone fractures in susceptible populations, hypomagnesaemia and rebound acid hypersecretion syndrome. Rare or very rare adverse effects of PPIs are listed to include subacute cutaneous lupus erythematous and tubulointerstitial nephritis and the British Society of Gastroenterology suggest an increased risk of spontaneous bacterial peritonitis in cirrhotic patients. Please see the BNF or the product's SPC for the full list of side effects. Therefore, clinical judgement should be used on an individual basis to assess the risks and benefits of long-term PPI use and included in shared decision-making discussions, with the lowest effective dose continued where appropriate.

## Lifestyle measures

Some lifestyle measures may help improve symptoms for conditions such as dyspepsia and/or reduce the risk of gastrointestinal bleeding. These include:

- Weight loss if overweight or obese
- Avoiding trigger foods and drinks. These could include rich, spicy, or fatty foods, coffee, cola and chocolate.
- Eating smaller, regular meals and not eating 3-4 hours before going to bed, where possible.
- Stopping smoking.
- Reducing alcohol consumption to within recommended limits.
- Manage stress and anxiety.

## Interactions:

See BNF/SPC for list of drug interactions.

Conflicting evidence for the interaction between omeprazole/esomeprazole and clopidogrel (see MHRA alert for more detail)

## Medication review recommendations

- Review other medication for which may possibly cause or exaggerate dyspepsia, considering stopping or reducing if possible and appropriate. These include alpha-blockers, anticholinergics, calcium-channel blockers, corticosteroids, nitrates, non-steroidal anti-inflammatories (NSAIDs), theophylline and tricyclic antidepressants.
- Offer annual reviews, or more often if appropriate, to those needing long term management of dyspepsia.
- Review long-term PPI usage at least annually conducting a risk vs benefit review of PPI, exercising caution in those patients with other risk factors for bone fractures and/or *Clostridioides difficile* infection.
- If a medication that increases bleed risk is stopped, re-review the need for the PPI. E.g. if PPI used for NSAID gastroprotection, and no longer needing NSAID, stop PPI.
- Encourage patients to report side effects.
- If deciding to stop PPI/change to when required (PRN) use, advise patient of possible rebound acid hypersecretion. Advise gradual tapering over several weeks, using antacids if needed during this time.
- Consider adding indication to PPI directions. This may help decision-making when consider deprescribing e.g. on hospital admission.

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## Identify the indication for the PPI

Prophylaxis against medication known to cause ulcers/bleeding use (past or current), endoscopy reports, history of heartburn, etc.

Unclear/ unknown indication

Acute treatment completed (see next page for recommended durations):

- Peptic ulcer disease treated (H.Pylori/NSAID)
- Oesophagitis healed, symptoms controlled
- Used for prophylaxis but causative agent stopped e.g. NSAID, DOAC (see next page)

Mild to moderate GI symptoms without endoscopy or proven erosions

Asymptomatic for 2 weeks or more

Hiatus Hernia or GORD

**Valid Indication**

(Refer to NICE CG184)

- Barrett's oesophagus
- Severe oesophagitis
- Oesophageal peptic stricture
- For gastroprotection in high-risk patients prescribed other medicines that increase risk of ulceration/bleeding*
- History of a bleeding GI ulcer with an unclear cause
- Zollinger-Ellison syndrome
- Short bowel syndrome
- Palliative patients (symptom control)

Continue PPI long-term

## Recommend de-prescribing

Ensure lifestyle interventions are in place (see above)

Stop the PPI, reduce the dose, or change to PRN (taper dose if concerned about rebound symptoms)

## Monitor at 4-8 weeks

Check for symptoms including heartburn, epigastric pain and weight loss/loss of appetite

**Significant return of symptoms**:

- Revert back to lowest effective dose.
- If continuing on PPIs, ensure the PPI use is reviewed annually as per NICE guidance.
- Consider testing for H.*pylori* (omit PPI for 2 weeks)

**No or minimal symptoms**:

- Change or continue to use PRN/stop PPI
- Switch to OTC antacids/alginates
- Lifestyle interventions

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| Indication | Typical daily dose ( See NICE CG184 for details, except where indicated) |
|---|---|
| **Barrett's oesophagus** | Omeprazole or Esomeprazole 20-40mg daily, or lansoprazole 30mg daily (titrate dose as needed to ensure no breakthrough symptoms) long-term. |
| **Oesophageal strictures** | Omeprazole 20-40mg, or Lansoprazole 15-30mg long term. |
| **GORD/dyspepsia** | Omeprazole 20-40mg or Lansoprazole 30mg for 4-8 weeks then review stopping (prescribe at lowest effective dose if required e.g. Omeprazole 10mg daily). |
| **Oesophagitis/Gastritis** | Omeprazole 20-40mg or Lansoprazole 30mg for 8 weeks to aid healing (maybe required long-term). Use omeprazole 40mg BD or Esomeprazole 20-40mg for endoscopically proven severe oesophagitis (LA grade C/D) or if refractory to initial treatment. |
| **Ulcers** (duodenal, gastric, NSAID associated) | Omeprazole 40mg or Lansoprazole 30mg for 4-8 weeks (long-term if NSAID continuing) then review. Consider re-scoping. If symptoms recur, restart PPI at the lowest effective dose. Esomeprazole 40mg if previously on PPI. |
| **Prophylaxis** (see table below) | Omeprazole 10-20mg or Lansoprazole 15-30mg whilst taking the drug, stop the drug if possible. Note: medicines listed below are known to cause peptic ulceration/increase bleeding risk. Other medicines e.g. bisphosphonates can cause reflux. |
| **H *pylori* treatment** | Omeprazole 20-40mg twice daily for 7 days (in addition to H pylori eradication antibiotics). |
| **Zollinger-Ellison Syndrome** | Omeprazole 20-120mg or Lansoprazole 60-120mg in two divided doses (adjusted to response) long term. |
| **Pancreatic enzyme replacement therapy** | Omeprazole 20mg – 40mg twice daily dose. Twice daily dosing (morning and evening) with PPI is often recommended to optimise therapy over a 24-hour period (See UBHW PERT clinical guideline) |

## *High risk patients - When to consider co-prescribing gastroprotection:

NSAIDs, antiplatelets, anticoagulants, corticosteroids and selective serotonin reuptake inhibitors are the main medications associated with GI bleed risk. Individual additional patient risk factors will determine if gastroprotection may be required. *Please note this list is not exhaustive and a comprehensive review of all patient risk factors should be undertaken to help determine the patient's need for* gastroprotection

**NSAIDs**

Moderate and high-risk patients → Gastroprotection required
(Moderate/high risk are: 1-2 risk factors, or previous complicated ulcer, or elderly, or patients with osteoarthritis and rheumatoid arthritis)
Low-risk patients = No risk factors → Gastroprotection not required

What are the NSAID GI risk factors?
Patients aged over 65, high dose or prolonged use of NSAID, history of gastroduodenal ulcer/perforation or GI bleeding, significant comorbidity (e.g. cardiovascular disease, hepatic or renal impairment, diabetes, hypertension), heavy smoking, excessive alcohol consumption, previous adverse reaction to NSAIDs, concomitant use of medications that are known to increase likelihood of upper GI bleeds, chronic low back pain/axial spondyloarthiritis, psoriatic arthritis, peripheral spondyloarthritides.

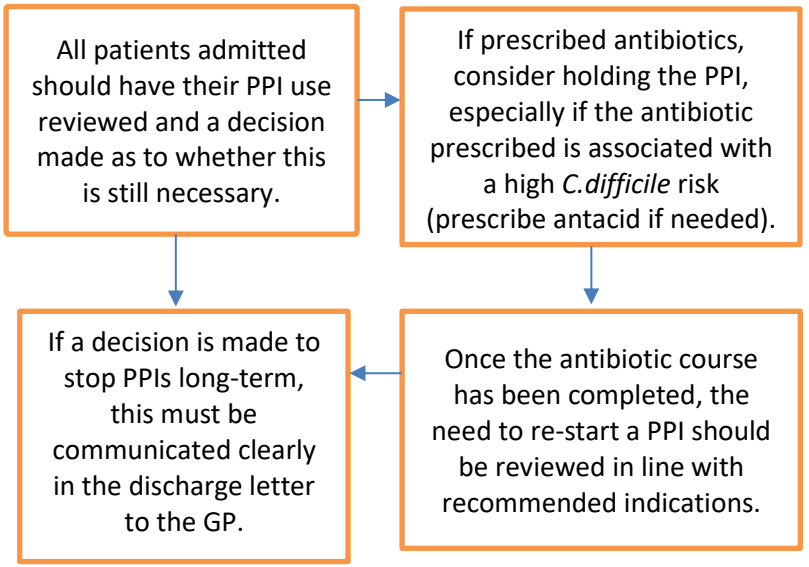
**Antiplatelets**

Gastroprotection should be considered alongside antiplatelets in patients: Taking high-dose aspirin, taking clopidogrel, who are elderly, history of gastroduodenal ulcer/perforation or GI bleeding, have a H.*Pylori* infection, taking concomitant use of medication with GI bleed risk (see list above)

**Anticoagulation, corticosteroids, selective serotonin reuptake inhibitors:**

Gastroprotection should be considered alongside these medications in patients with: History of gastroduodenal ulcer/perforation or GI bleeding, concomitant use of medication with GI bleed risk (see list above), older age, serious comorbidity (e.g. advanced cancer)

## Patients admitted to hospital

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