# UPDATE
## Module 1663

**This module covers:**

- When gastroprotection is needed
- Symptoms of people needing gastroprotection
- Medicines used to provide gastroprotection
- Treatment of specific conditions

**JULY »**
**Gastrointestinal**

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**Online-only module for Update and Update Plus subscribers*

# Gastroprotection

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The prescribing of medication to protect the stomach from excess acid production has been steadily increasing. In fact, the drug with the greatest increase in the number of items dispensed in 2011 over that dispensed in 2010, was omeprazole.[1] This could be for a number of reasons, including increased obesity and increased prescribing of non-steroidal anti-inflammatory drugs (NSAIDs), steroids and other reflux-causing medications.

There has been no change to the gastroprotection range since Nice guidelines were published in 2004, but proton pump inhibitors (PPIs) are now available over the counter and there have also been changes to prescribing advice following the results of post-marketing studies.

## Who needs gastroprotection?

There are three main reasons for the prescribing of gastroprotective agents:[2]

- protection from the side effects of concurrent medication such as NSAIDs and corticosteroids, which increase the risk of bleeding
- alleviation of the side effects of concurrent medication, such as bisphosphonates, nitrates and theophylline
- control of a medical condition: heartburn and indigestion, *Helicobacter pylori* (*H.pylori*) eradication, upper GI bleed, Zollinger-Ellison syndrome, Barrett's oesophagus, oesophageal peptic stricture.

Gastroprotective agents should always be prescribed for high-risk patients, which includes those with previous peptic ulcer disease, those aged over 65 years on long-term NSAIDs, steroids or clopidogrel, those on long-term medications that increase bleeding risk, and patients with serious co-morbidity.[3]

There are individual Nice guidelines indicating when gastroprotection should be prescribed for certain conditions. They include PPI use in rheumatoid arthritis, low back pain and osteoarthritis when long-term NSAIDs and/or corticosteroids are prescribed.


**Lansoprazole is best taken in the morning, 30 minutes before food; capsules can be opened up and the contents sprinkled onto food or dissolved in a small amount of water**

While there has been no change to the 2004 Nice guidelines, various studies have highlighted further evidence that has affected certain individual products. For example, a PPI should only be prescribed with clopidogrel if it is essential, with lansoprazole being the drug of choice. There is also evidence of increased fracture risk with PPIs in certain patients.

## Symptoms

About 40 per cent of the adult population suffer some sort of upper gastrointestinal tract (GIT) symptoms in any one year,[4] with about 50 per cent of those self-medicating.[4] There can be an identifiable cause (non-functional dyspepsia) but functional dyspepsia, where no causal disease is identified, is more common. Symptoms vary, but include upper abdominal discomfort, heartburn, retrosternal pain, acid reflux, nausea, vomiting, bloating and early satiety.

Gastro-oesophageal reflux disease (GORD) is where acid reflux into the oesophagus occurs, producing symptoms interfering with quality of life.[5] This term is used to encompass all diseases caused by gastro-oesophageal reflux.[4]

Differential diagnoses include cardiac problems, motility disorders of the GIT, peptic ulcer disease, dysphagia, irritable bowel syndrome, gastric or oesophageal cancer, asthma and non-cardiac chest pain.

Alarm or red-flag symptoms indicating the need for GP referral are shown in box 1 (page 2, top, right).

## Medication

A range of medication can be used to control

gastric acid secretion, each acting at different stages in the acid production cycle.

### Antacids and alginates

Antacids contain sodium, calcium or magnesium salts, which react with stomach acid to neutralise it. They are suitable for intermittent treatment and exacerbations. Calcium-containing products can cause rebound acidity and magnesium can cause diarrhoea and aluminium constipation. Liquids act faster, whereas tablets last for longer. Some preparations contain high levels of sodium, so should be avoided in cardiovascular and kidney disease, or where fluid retention may be a problem. Low-sodium content preparations include Maalox.

Alginates contain sodium alginate, sodium bicarbonate and calcium carbonate. They react with gastric acid to form a viscous gel that sits on top of the stomach contents, protecting the oesophagus when reflux occurs. This layer can also prevent acid reflux. High sodium content may also be a problem with alginate preparations. Low-salt preparations contain less than 1mmol of sodium per tablet or 10ml dose and include Gastrocote and Topal tablets. Gaviscon and Gaviscon Advance contain more than 2mmol of sodium per 5ml.

Alginates and antacids can interfere with the action of enteric-coated tablets and other preparations designed to pass through an acidic stomach and dissolve in the lower GIT. They should not be taken at the same time as tetracyclines, iron supplements and ulipristal. Alginates and antacids could potentially alter the absorption of many other medications as well; it is prudent to advise a two-hour gap between the two.[3]

### H2-receptor antagonists

H2-receptor antagonists (H2RAs) are competitive inhibitors of the H2-receptors on the parietal cells in the stomach lining. They work best for nocturnal symptoms; a dose of ranitidine 150mg is effective for about 12 hours.[7] Ranitidine is taken either twice daily or at night and can be taken with or without food.

Cimetidine inhibits cytochrome P450 so interacts with many other medicines, notably increasing effects of warfarin, theophylline, phenytoin, amiodarone, carbamazepine and sodium valproate. It can also cause gynaecomastia and loss of libido.[8] Ranitidine does not have this effect.

Famotidine is available as an over-the-counter preparation combined with two antacids (PepcidTwo), and ranitidine is available as a pharmacy medicine.

### Proton pump inhibitors

Proton pump inhibitors (PPIs) are prodrugs that are converted to sulfonamide at acidic pH. Sulfonamide combines irreversibly with sulphydryl groups on the H+/K+ ATPase (hydrogen/potassium adenosine triphosphatase) enzyme, and inhibits the gastric proton pump in the parietal cells. This stops the release of the hydrogen ions (protons) into the stomach.

Although they can give symptom relief shortly after taking, PPIs take three to four days to reach maximum effect.[7] Antacids can be recommended at the start of treatment. Nice recommends PPIs as first-line treatment for uninvestigated dyspepsia, GORD and gastric and duodenal ulcers,[9] as they are more effective than H2RAs.

There is little difference between the PPIs, although esomeprazole is more effective than omeprazole,[8] but neither should be prescribed with clopidogrel: if a PPI is required, then lansoprazole should be used.

Lansoprazole is best taken in the morning, 30 minutes before food;[10] the presence of food does not affect availability of omeprazole.[11] Lansoprazole capsules can be opened up and the contents sprinkled onto food or dissolved in a small amount of water.[10]

PPI drug interactions include digoxin, theophylline and tacrolimus, and side effects include gastrointestinal disturbance, headache, rash and dizziness, but they are generally well tolerated. Caution is required in liver disease, pregnancy and breastfeeding.

Long-term use of PPIs can increase the risk of hip fractures, which is further increased in smokers,[12] so patients should be advised to ensure they have adequate calcium and vitamin D intake. Long-term use can also cause hypomagnesaemia, so it is prudent to monitor magnesium levels, especially when taken with digoxin or diuretics.[13]

There has been some conflicting evidence around PPIs and infection risk, specifically *Clostridium difficile* and pneumonia, due to lower acid levels reducing non-specific defence against ingested pathogens.[2]

### Other agents used in gastric disease

Simeticone is an antifoaming agent and is used to relieve flatulence, although there is little evidence for benefit.[12]

Misoprostol, a prostaglandin-E (PGE) analogue inhibiting gastric secretion,[12] is used to reduce ulceration risk with NSAIDs and is thought to be more effective than H2RAs. It is available combined with diclofenac or naproxen. It should not be used in pregnancy and used with caution in women of child-bearing age.

Sucrulfate is a cytoprotective agent, which has a specific affinity for ulcer sites, and is recommended in stress ulceration prophylaxis.[3]

Bismuth acts by coating the stomach lining to prevent irritation.

## Specific conditions

Nice has guidelines for the following conditions – an MUR should be conducted first and lifestyle advice also given.[8,9]

*Box 1. Red-flag symptoms*

In the community pharmacy setting the following red flag symptoms indicate the need for GP referral:[6]

- unintentional weight loss
- anaemia
- gastrointestinal bleeding
- pain on swallowing
- persistent vomiting, with or without blood
- previous ulcer or surgery
- epigastric mass
- jaundice
- children aged under 16 years
- anyone aged over 45 years with new or recently changed symptoms

## Tips for your CPD entry on gastroprotection

*Reflect* **For which patient groups should gastroprotection always be prescribed? What are the side effects of proton pump inhibitors? How are gastric and duodenal ulcers treated?**

*Plan* **This article describes gastroprotection and when it should be used. It includes information about gastrointestinal tract symptoms and the patients at high risk of developing these symptoms. Gastroprotective medicines, the Nice guidance for their use and advice that pharmacists can give to patients are also discussed.**

*Act* **Read the article and the suggested reading, then take the 5 Minute Test. Update and Update Plus subscribers can then access their answers and a pre-filled CPD logsheet.**

**Find out more about dyspepsia from the NHS Choices website**
tinyurl.com/gastroprotection1
**Read more about the drugs used in the management of dyspepsia, *Helicobacter pylori* infection and NSAID-associated ulcers in the BNF, Section 1 Gastrointestinal system**
**Read the MUR tips for antacids and alginates, H2 antagonists and PPIs on the C+D website**
tinyurl.com/gastroprotection2

*Evaluate* **Are you now confident in your knowledge of the patients at risk of developing GI tract symptoms and the drugs used in gastroprotection? Could you give advice about OTC treatments and lifestyle to patients suffering from dyspepsia?**

### Uninvestigated dyspepsia

A full-dose PPI should be trialled for one month, whether further investigation is required or not. The dose can be doubled in GORD if there is no response, and an H2RA or prokinetic (eg metoclopramide) added if needed.

### Gastric and duodenal ulceration

A large proportion of gastric ulcers are caused by *H.pylori*. Following a positive *H.pylori* test, treatment is a triple-therapy course of two antibiotics and a PPI for one week. In previously failed treatment, four agents are used. After eradication of *H.pylori*, a low-dose PPI can be used if symptoms persist, then stepping down to self-care with antacids or alginates as needed.

Following a negative *H.pylori* test, patients with gastric ulcer chould be given a full-dose PPI for one to two months, plus an endoscopy, and then referral to secondary care if there is no response. Endoscopy or secondary care referral are not indicators for duodenal ulceration.

### Ulcers associated with NSAIDs

The NSAID should be withdrawn, a full-dose PPI given for two months, and then review and step down.

### Non-ulcer dyspepsia

Following a negative *H.pylori* test or positive test and eradication with no response or relapse, a low dose PPI or H2RA should be given for one month, then as required with regular review.

In all cases, upon resolution and where any ulceration is not medication-related, treatment can be stepped down to the lowest dose controlling the symptoms. Any symptoms that do then occur can be treated with antacids or alginates as needed. However, in hard-to-treat cases, a PPI and an H2RA can be used in combination.

## Advice pharmacists can give

Whatever the underlying cause, lifestyle advice to help reduce symptoms should be given and includes:

- avoiding known trigger factors, such as alcohol, spices, caffeine and fatty foods
- avoiding bending over shortly after eating
- avoiding large meals shortly before bed
- raising the head of the bed
- smoking cessation
- avoiding tight clothing round the abdomen
- weight reduction, as obesity increases pressure on the oesophageal sphincter.

It is worth noting that stress and depression can be the cause of reflux and heartburn. Reflux is also common in pregnancy, due to the pressure of the foetus in a small area – Gaviscon is usually used, but in severe cases omeprazole can be prescribed.

Pharmacists may receive frequent over-the-counter requests for antacids, H2RAs and PPIs as heartburn and reflux are common problems. The majority of cases are usually quite short in duration, but red-flag signs should always be referred. Anyone over 45 years presenting with new onset symptoms lasting more than four weeks, or whose symptoms have changed, must also be referred to their GP.

Antacids, alginates and H2RAs can be recommended for discrete attacks of heartburn, but PPIs are better for recurrent symptoms.[6] Omeprazole was the first PPI to be made available over the counter for use in certain situations.[6] The starting dose is two tablets, once daily for three to four days to achieve symptom relief, then stepped down to one daily. Pantoprazole should be taken around 30 minutes before food,[14] and complete symptom relief is seen within seven days. Both should not be used for longer than four weeks without GP consultation.

Community pharmacists are also in an ideal position to review gastroprotection use, through MURs for example, ensuring patients prescribed short courses do not remain taking them unnecessarily, and that those taking them regularly have their symptoms under control.

### 5 minute test

■ Sign up to take the 5 Minute Test and get your answers marked online: chemistanddruggist.co.uk/update

## Take the 5 Minute Test

**1.** Nice has individual guidelines for PPI use in rheumatoid arthritis, low back pain and osteoarthritis.
**True or false?**
**2.** Around 70 per cent of adults suffer some sort of upper gastrointestinal tract symptoms in any one year.
**True or false?**
**3.** Dyspepsia with an identifiable cause is more common than dyspepsia where no causal disease is found.
**True or false?**
**4.** Antacids containing calcium and magnesium often cause constipation.
**True or false?**
**5.** Low-salt antacid preparations contain less than 1mmol of sodium per tablet.
**True or false?**
**6.** Common side effects of ranitidine include gynaecomastia and loss of libido.
**True or false?**
**7.** Nice recommends PPIs as first-line treatment for uninvestigated dyspepsia and GORD.
**True or false?**
**8.** Omeprazole and lansoprazole should both be taken with or after food.
**True or false?**
**9.** PPI drug interactions include digoxin, theophylline and tacrolimus.
**True or false?**
**10.** Long-term use of PPIs is associated with an increase in hip fracture risk.
**True or false?**

## References


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7. Zantac Tablets 150mg Summary of Product Characteristics, GlaxoSmithKlineUK.
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