

This Medicines Information Leaflet is produced locally to optimise the use of medicines by encouraging prescribing that is safe, clinically appropriate, and cost-effective to the NHS.

Prescribing Guidelines for Proton - Pump Inhibitors & *Helicobacter pylori* eradication in adults

The management of non-variceal upper gastrointestinal bleeding (UGIB), dyspepsia and gastro-oesophageal reflux disease can be optimised with the appropriate use of proton-pump inhibitor (PPI) therapy. In terms of efficacy or adverse effects there are few differences among the licensed PPIs. The formulary choice of PPI in this Trust is based on established clinical experience and cost in primary care. Generic omeprazole and lansoprazole capsules are the oral PPIs of choice in this Trust. Omeprazole is the intravenous PPI of choice.

For inpatients on such medications, these can be substituted using recommendations from the Therapeutic Substitution and Suspension [MIL](#). Patients should not be referred to their GP for initiation of non-formulary PPIs. Esomeprazole sachets and orodispersible lansoprazole tablets are available but for restricted indications as per the [OUH formulary](#)

H₂-receptor antagonists may be considered for patients unsuitable for PPI therapy. If you are unsure, please contact your ward pharmacist to discuss use and for the current formulary choice.

Intravenous (IV) PPIs

Pre-endoscopy

Recommendations from the BSG-led multi-society consensus on management of acute UGIB varies from the conservative guidelines set out by NICE. Whilst PPIs can reduce the need for endoscopic therapy, there is little evidence to suggest that PPI administration affects re-bleeding or mortality rates, though this has tended to be in studies where expedited endoscopy has been available. However, in a time- and staff-pressured health system, if a non-variceal UGI bleed is suspected and the timing of any endoscopy procedure is unclear, or is likely to happen beyond 6 hours of the patient's presentation, off-license use of intermittent IV PPI therapy (omeprazole 40mg IV BD) pre-endoscopy, without approval from the

gastroenterology team, is reasonable. Endoscopy should be ordered prior to second dose of IV PPI.

Patients presenting with UGIB should not have low-dose aspirin (75 - 150mg) stopped due to increased risk of cardiovascular and cerebrovascular events. Specialist advice should be sought regarding discontinuation of other antiplatelets/anticoagulation if patients have had recent coronary, intracranial, or carotid stents. Anticoagulation effects of warfarin can be reversed with vitamin K. Andexanet alfa is available for the reversal of apixaban and rivaroxaban as per the [MIL](#). Idarucizumab is available for reversal of bleeding in patients taking dabigatran. Medications which lower blood pressure should be suspended.

Other medications which precipitate bleeding should be suspended and include:

- NSAIDs (particularly naproxen, ketorolac, piroxicam. Ibuprofen is lower risk)
- SSRIs (citalopram, sertraline, fluoxetine) and SNRIs (duloxetine, venlafaxine)
- Carbocisteine
- Bisphosphonates (e.g. alendronic acid)

Patients on combinations of these agents can see up to 6-fold increases in bleeding risk

Post-Endoscopy

IV PPIs are indicated post-endoscopy in proven peptic ulcer disease or if stigmata of recent haemorrhage, regardless of aetiology. Guidance will often be offered in the endoscopy report.

For the **post-endoscopic** management of peptic ulcers that have required endoscopic therapy, an omeprazole infusion (80mg bolus then 8mg/hour for 72 hours) has traditionally been used. However, BSG-led consensus suggests that intermittent IV omeprazole therapy (omeprazole 40mg IV BD) is comparable in efficacy to omeprazole infusion, and is more cost-effective, though this remains unlicensed. This intermittent IV dosing regimen is recommended by the OUH gastroenterology

team. Further details for administration can be found through [Medusa](#).

Discharge

At discharge, guidance on ongoing oral PPI therapy is outlined below. Patients with proven peptic ulcer disease should undergo *H. pylori* testing if not done endoscopically and complete *H. pylori* eradication if positive (see below).

Further information on the management of **variceal** bleeding should be under the guidance of a hepatologist and in line with [BSG guidelines](#)

IV PPIs – other indications

Intravenous PPIs can also be given on a restricted basis to the following patients:

- Stress ulcer prophylaxis: as per local critical care guidelines
 - Zollinger-Ellison syndrome: 60mg OD (initially, then adjust according to response) where patient is nil by mouth
 - Perforated gastric or duodenal ulcer: 40mg BD*
 - Short bowel syndrome: 40mg BD*
 - Two test doses of 40mg IV pantoprazole for home parenteral nutrition patients prior to discharge*
- * - these indications are off-label

Pharmacy will not dispense IV PPIs other than for the above indications.

IV PPIs are **not** indicated for acute acid suppression, or for nil-by-mouth patients previously taking long-term oral PPI therapy unless recommended by a gastroenterology specialist.

Oral PPI therapy recommended regimens:

Doses as per BNF, equivalent doses available via [BNF](#)

	Standard dose	High dose	Low dose
Omeprazole	20mg daily	40mg daily	10mg daily
Lansoprazole (including severe oesophagitis)	30mg daily	30mg twice daily	15mg daily

Short-term treatment with standard dose PPI:

- Healing severe oesophagitis (8 weeks) – if initial treatment fails, consider high dose treatment
- Gastro-oesophageal reflux disease (4 or 8 weeks) – if symptoms recur thereafter use lowest effective dose
- Dyspepsia (4 weeks) (unlicensed)
- Benign gastric ulcers (8 weeks)
- NSAID-associated ulceration (4 weeks, increased to 8 weeks if not fully healed)
- Post-banding of oesophageal varices (continue until eradicated/healed under specialist supervision from hepatology team)

Long-term treatment with standard dose PPI:

- Barrett's oesophagus
- Complicated oesophagitis (strictures, ulceration, haemorrhage)
- Oesophageal reflux that relapses on stopping therapy
- High risk factors for GI bleeding that require long-term NSAID use e.g. elderly

Exceptions to standard dose PPI regimens:

Short term treatment:

- Healing of perforated peptic ulcer: omeprazole 40mg twice daily until repeat OGD, treatment should last at least 4 weeks
- Severe oesophagitis refractory to initial standard dose treatment: omeprazole 40mg twice daily for 8 weeks

Long term treatment:

- High output stomas (more than 1500ml per day) or short bowel: omeprazole 40mg BD is recommended
- Zollinger Ellison syndrome: range from omeprazole 20-120mg (doses above 80mg/day should be given in 2 divided doses)
- Treatment of perforated peptic ulcers: omeprazole 40mg BD
- Omeprazole 10mg doses recommended in long-term management of acid reflux disease and functional dyspepsia

Adverse Effects

PPIs are generally well tolerated. Common side effects include gastro-intestinal disturbances and headache. Caution should be taken in patients with severe liver disease, pregnancy, and breast-feeding.

Widespread usage and long-term therapy, especially at higher doses, and particularly in the elderly, has shown an association with several adverse effects. These include electrolyte disturbances such as hyponatraemia and hypomagnesaemia. There are observational studies associated with an increased risk of renal disease, fractures, and community-acquired pneumonia. Co-administration of ulcer-healing drugs in addition to antibiotics increases the risk of *Clostridioides difficile* infection (CDI) two to three-fold. PPIs should be reviewed on admission in all patients and especially in those patients at high risk of CDI. The risk of antibiotic associated colitis is uncommon with antibiotics and PPI combinations used as part of *H. pylori* eradication regime. Gastric acid suppression has also been associated with other GI infections i.e. salmonella and campylobacter. For further information on CDI refer to Trust Guidelines [here](#).

PPIs may mask the symptoms of gastric cancer and particular care is required in those presenting with alarm features:

- Gastrointestinal bleeding
- Nausea and/or vomiting
- Abdominal pain

- Unexplained weight loss (over 4.5kg over 3 months)
- Dysphagia

Strong consideration should be given to excluding upper GI malignancy before prescribing or at the time of prescribing.

General Tips for PPI prescribing

- Review therapy for all patients prescribed PPIs after 8 weeks (2 weeks if cardiac trial), with a view to "step down" and/or "step off" treatment
- All high dose prescriptions should be reviewed regularly, and the dose reviewed as above. This includes admission to secondary care
- The GP should be notified of the indication and planned duration of treatment through documentation on discharge summary
- The dose of PPI, if recommended following endoscopy, should be clearly stated on the endoscopy report
- Patients should be counselled on lifestyle and dietary changes as appropriate for ulcer healing such as smoking cessation, reduction in alcohol intake, weight reduction, and necessity of OTC or prescribed NSAIDs
- NSAIDs are associated with a three- to four-fold increased risk of peptic ulcer development. The risk doubles with concomitant use of low-dose aspirin and there is a five- fold increase in risk if dual anti-platelet therapy is taken
- SSRIs in conjunction with NSAIDs increase the risk of an upper GI bleed six-fold. The need for these drugs should be reviewed regularly (minimum every 6 months) and they should be withdrawn, wherever possible, if an ulcer occurs.
- Cyclo-oxygenase-2 inhibitors (COX-2 inhibitors) have been associated with a reduction in ulcer occurrence and GI intolerance, compared to full doses of non-selective NSAIDs. However, in those at high risk (e.g. previous ulceration) a PPI should be co-prescribed. COX-2 inhibitors are also associated with an increase in thrombotic events (e.g. myocardial infarction and stroke) and are therefore contra-indicated in patients with ischemic heart disease, peripheral arterial disease, moderate to severe heart failure or cerebrovascular disease.
- Corticosteroids alone are not associated with an increase in the risk of peptic ulcer. However, they can exacerbate NSAID-induced ulceration. There is no indication for PPI cover in patients prescribed monotherapy of corticosteroids, aspirin, warfarin, DOACs, or SSRIs.

Helicobacter pylori

Helicobacter pylori (*H. pylori*) is a causal factor in many upper gastrointestinal conditions, from minor dyspepsia to gastric cancer, and its eradication is worthwhile. However, eradication therapy fails in some patients. It is therefore

important to make an individualised assessment of the balance between the risk of continued colonisation by *H. pylori*, with long-term administration of a PPI, and potential antibiotic-related complications. Locally, *H. pylori* infection can be detected from biopsy (histology or CLO test), by serology, breath-testing, or faecal antigen testing.

Offer *H. pylori* eradication to those with a positive *H. pylori* test AND any of the following clinical correlates:

- Peptic ulcer disease (gastric/duodenal)
- Dyspepsia
- MALT lymphomas
- Unexplained iron deficient anaemia
- ITP
- After (endoscopic) gastric resection of early gastric neoplasia
- First degree relatives of patients with gastric cancer

H. pylori and NSAID use are independent risk factors for GI bleeding and ulceration. In patients already taking NSAIDs, eradication is unlikely to reduce the risk of NSAID-induced bleeding or ulceration. However, patients with a history of peptic ulcer disease or dyspepsia and *H. pylori* positive who are about to start long term treatment with a non-selective NSAID, eradication may reduce the overall risk.

H. pylori eradication regimens

The importance of treatment adherence should be discussed with the patient. Treatment failure is usually due to antibacterial resistance and/or poor adherence.

Eradication regimens must be administered orally or via a nasogastric tube. Eradication therapy should not be started until the patient can complete the 14-day course via either of these routes.

If the ulcer is large or complicated by hemorrhage or perforation, treatment should continue for a further 4 weeks or until repeat OGD/endoscopic treatment intervention or surgery (if required)

OUH standard is to offer confirmation of *H. pylori* eradication to all those with peptic ulcer (gastric or duodenal) 6-8 weeks after beginning treatment, depending on the size of the lesion. A repeat endoscopy should also be offered to those with gastric ulcer and *H. pylori* within 8 weeks of the index procedure.

A ¹³C-urea breath test should be booked via endoscopy and followed up via endoscopist (they are not routinely performed in primary care). ¹³C-urea breath tests should not be performed within 4 weeks of completing treatment with an antibacterial or within 2 weeks of a PPI.

The *H. pylori* Eradication PowerPlan  should be used on EPR with first/second line options selected as appropriate. The current options reflect NICE recommendations and availability and have been ratified

on Trust antimicrobial guidelines. Patients who fail to respond to second line treatment should be referred to Gastroenterology and Microbiology/ID for further treatment discussion.

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Review date: September 2028