MIL

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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.** All other PPIs (including esomeprazole) are non-formulary and are not stocked. Patients should not be referred to their GP for initiation of non-formulary PPIs.

Intravenous PPIs:

IV PPIs are indicated in proven non-variceal UGIB or stigmata of recent haemorrhage where they have been shown to enhance platelet aggregation and clot formation to promote haemostasis and prevent re-bleeding.

Current evidence suggests that the use of acid suppression therapy (PPIs/H_2-receptor antagonist) before endoscopy offers little value in improving clinical outcomes for patients presenting with suspected non-variceal UGIB. In line with current NICE guidance the OUH Trust does not recommend the pre-emptive use of IV acid-suppression therapy before endoscopy.

For major peptic ulcer bleeding (following endoscopic treatment) an IV loading dose of omeprazole 80mg, followed by a continuous infusion of 8mg per hour for 72 hours should be given. This IV regimen is unlicensed but NICE approved and should be prescribed by the endoscopist after endoscopic therapy. The Omeprazole infusion for peptic ulceration PowerPlan should be used on ePMA. Further details of administration can be found in the IV monograph at: OUHi > Pharmacy > Injectables

On completing the infusion patients should receive oral omeprazole 40mg daily (high dose) for 8 weeks, and *H. pylori* eradicated if positive. **This is essential if there are complications e.g. haemorrhage or perforation or surgery is required.**

Drugs that can precipitate bleeding or lower blood pressure should be stopped in patients who present with an UGIB. Once haemostasis has been achieved patients on low dose aspirin for secondary prevention of vascular events should be continued. The risks and benefits of continuing other NSAIDS, clopidogrel, ticagrelor and anticoagulants should be discussed at discharge.

Further information regarding the management of non-variceal UGI bleeding can be found at:
OUHi > Gastroenterology and Hepatology > Document Library

Intravenous PPIs – other indications:

Intravenous omeprazole can be administered as bolus doses, the use of which is restricted to the following patients:

- **Intensive care patient following failure of ranitidine:** 40mg once a day
- **Zollinger-Ellison syndrome or perforated oesophagus:** 40mg twice daily (unlicensed)
- **Perforated gastric or duodenal ulcer:** 40mg twice daily

IV PPIs are **not** indicated for acute acid suppression, acute GI haemorrhage prior to endoscopy or for nil-by-mouth patients previously taking long-term oral PPI therapy.

In patients in whom early endoscopy may be delayed or where endoscopic expertise is unavailable within 24 hours or when the patient is more likely to be bleeding from a non-variceal source or high risk lesion (haematemesis), a once only dose of PPI (oral if possible) can be given.

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

Oral PPI therapy recommended dosing:

Short term treatment with standard dose PPI (Table 1):

- Healing severe oesophagitis (8 weeks) – if initial treatment fails consider high dose treatment
- Gastro-oesophageal reflux disease (4 – 8 weeks) – if symptoms recur thereafter use lowest effective dose
- Dyspepsia (4 weeks)
- Benign gastric and duodenal ulcers (4–8 weeks)
- NSAID–associated ulceration (8 weeks)
- Therapeutic trial in cardiac patients (2 weeks) - Omeprazole 40mg daily/ lansoprazole 30mg daily is recommended

- Post banding of oesophageal varices (continue until eradicated/ or continue if reflux symptoms which can sometimes occur post banding)

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

Long-term treatment with standard dose PPI (see Table 1):

- Barrett's oesophagus
- Hypersecretory conditions e.g. Zollinger-Ellison syndrome
- 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 (patients over 65 years of age)
- Severe oesophagitis LA grade C and D
- High output stomas (>1500ml/day) or short bowel- omeprazole 40mg twice daily is recommended

Adverse Effects

PPIs are generally well tolerated. Common side effects include gastro-intestinal disturbances and headache. Particular 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 seen an association with a number of adverse effects. These include **electrolyte disturbances such hyponatraemia and hypomagnesaemia**. There are observational studies associated with an increased risk of **renal disease, fractures, community-acquired pneumonia, and dementia.** Co-administration of ulcer-healing drugs in addition to antibiotics increases the risk of ***Clostridium difficile* infection (CDI)** two to three- fold. This is principally PPIs but also includes H_2-receptor antagonists. 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 refer to Trust Guidelines on CDI at:

OUHi > Infection Control > Document Library > CLOSTRIDIUM DIFFICILE

PPIs may mask the symptoms of gastric cancer and particular care is required in those presenting with “alarm features”. In such cases gastric malignancy should be excluded before treatment is commenced.

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 or by breath 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)
- Uninvestigated dyspepsia (‘test and treat’)
- Functional 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 NSAIDS 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 and 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 naso-gastric tube. Eradication therapy should not be started until the patient can complete the 7- day course via either of these routes.

There is normally no need to continue PPIs unless the ulcer is large or complicated by haemorrhage or perforation in which case treatment should continue for a further 3 weeks (a total of 8 weeks if endoscopic treatment intervention or surgery required).

Confirmation of *H. pylori* eradication should be offered to those with peptic ulcer (gastric or duodenal) 6-8 weeks after beginning treatment, depending on the size of the lesion. Retesting is unnecessary in functional dyspepsia. A ^{13}C-urea breath test should be booked via endoscopy (they are not routinely performed in primary care). ^{13}C-urea breath tests should not be performed within 4 weeks of treatment with an antibacterial or within 2 weeks of a PPI. A repeat endoscopy

should also be offered to those with gastric ulcer and *H pylori*.

The *H. pylori* eradication PowerPlan should be used on ePMA with first/second line options selected as appropriate. The current options reflect NICE recommendations and availability and have been ratified on microguide. Advice from a gastroenterologist should be sought if eradication of *H. pylori* is unsuccessful with second-line treatment.

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 on admission to secondary care.**
- **The GP should be notified of the indication and planned duration of treatment (via the 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 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 ulcers compared to full doses of non-selective NSAIDs and less gastro-intestinal intolerance. However, in those at high risk (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 ischaemic 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 corticosteroids alone.**

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