

Guidelines for the use of Proton Pump Inhibitors (PPIs) and the investigation of dyspepsia in Newcastle, Northumberland and North Tyneside

These guidelines were prepared by Gastroenterologists, General Practitioners and Pharmacists representing Newcastle, Northumberland and North Tyneside.

Choice of PPI

On the basis of cost (including likely trends in the foreseeable future), efficacy, side effect profile, speed of onset, potential for drug interactions, and the range of licensed indications the recommendations for the choice of PPIs is as follows:-

First choice PPI – omeprazole capsules, starting dosage 20 mg per day.

Second choice PPI – lansoprazole capsules, starting dosage 30mg per day.

The maintenance dosage is the minimum one which maintains adequate symptomatic relief.

If liquid form required, eg tube fed patients – lansoprazole orodispersible.

Parenteral formulation- omeprazole. (See notes on upper GI bleeding later in document)

Helicobacter Pylori Eradication

First line treatment Lansoprazole 30mg twice daily
 Amoxicillin 1g twice daily
 Clarithromycin 500mg twice daily

All given for 1 week. In primary care or for hospital outpatients this combination can be conveniently prescribed as Heliclear for 1 week.

Second line treatment (or for penicillin sensitive patients)

 Lansoprazole 30mg twice daily
 Clarithromycin 500mg twice daily
 Metronidazole 400mg twice daily

All given for 1 week.

Omeprazole 20mg twice daily may be used as an alternative to lansoprazole in the above regimens.

The Investigation of dyspepsia

Dyspepsia includes recurrent epigastric pain, heartburn and acid regurgitation, with or without bloating, nausea or vomiting.

1. Patients of any age with dyspepsia who also have chronic GI bleeding, progressive unintentional weight loss, dysphagia, persistent vomiting, iron deficiency anaemia, epigastric mass or a suspicious barium meal should be referred for endoscopy via the 2-week wait system.
2. Patients over the age of 55 with new onset, persistent dyspeptic symptoms should be referred for endoscopy via the 2-week wait system whether or not they have alarm features. **Note that although this recommendation contradicts NICE guidelines for the ‘Management of dyspepsia in adults in primary care’ they are fully consistent with NICE ‘referral guidelines for suspected (upper gastrointestinal) cancer’.**
3. Other patients should be tested and treated for HP, or failing this given a 1-month course of PPI. If this treatment fails to alleviate the patient’s symptoms, or if the symptoms recur, then refer for endoscopy via the open access endoscopy service.

Indications for the use of PPIs

Helicobacter Pylori (HP) +ve Duodenal ulcers

This accounts for 95% of duodenal ulcers and they should be treated by HP eradication. A test of the success of eradication is necessary if the patient remains symptomatic, if recurrent symptoms develop, or if the patient presented with complications and would otherwise require long-term therapy. A Carbon Urea Breath test is the preferred means of determining success of eradication. Serological testing has no role in this regard. Insufficient data is present on faecal antigen testing as yet to recommend it as a test of eradication. Carbon Urea Breath (CUB) testing is available at the Medical Physics Department at NGH and at Wansbeck Hospital and can be accessed directly by GPs. The CUB test should be delayed for 4 weeks after completion of eradication therapy and PPIs should not be taken in the 2 weeks beforehand. If eradication is confirmed no further treatment is necessary. If eradication has failed a second course of eradication therapy should be given. PPI maintenance is given if the patient remains HP +ve.

HP –ve duodenal ulceration.

This is usually associated with the use of non-steroidal anti-inflammatory drugs (NSAIDs). A two month course of a PPI is prescribed. Ideally the NSAID should be stopped during the course of ulcer healing. Refer to a Gastroenterologist if the patient is HP negative and not on NSAIDs as there may be an unusual cause such as Crohn's disease. Give a longterm PPI (omeprazole 20mg or lansoprazole 15mg per day) in those at serious risk of complications from continuing NSAID therapy.

Erosive duodenitis

In the absence of other evidence this is regarded as being within the spectrum of duodenal ulcer disease and treated as such.

Zollinger Ellison Syndrome

Patients with this condition should be referred for specialist management.

Benign Gastric ulceration (GU)

70% are HP positive with the remainder being NSAID associated. Biopsies are taken at the initial diagnostic endoscopy and HP status is determined by a rapid urease test.

HP+ve GU

A course of HP eradication is given followed by a 2-month course of PPI. Long-term treatment (omeprazole 20mg or lansoprazole 15 mg per day) is given if the patient needs to continue NSAIDs.

HP-ve GU

A PPI is given for 2 months with NSAIDs being stopped if possible. Long term PPI treatment (omeprazole 20mg or lansoprazole 15 mg per day) is given if the patient needs to continue NSAIDs long term.

Follow up of GU

Repeat endoscopy and biopsy is required until the ulcer is completely healed.

Prophylaxis of NSAID Therapy

COX 2 specific NSAIDs are now known to increase the incidence of vascular events in patients with underlying vascular disease and are contraindicated in this situation. In patients taking NSAIDs who would be at a high risk of complications consider co prescribing a PPI (omeprazole 20mg and lansoprazole 15 mg are both efficacious).

Gastro-oesophageal Reflux Disease (GORD) / Reflux Oesophagitis

PPIs are indicated in persistently symptomatic GORD along with lifestyle measures such as weight loss. 1 to 2 months treatment at the starting dosage should be followed by a step down approach so that the lowest dose to control symptoms is used. For some patients 'as required' use provides adequate symptomatic relief. For patients with complicated disease such as an oesophageal stricture or Barrett's

oesophagus continue starting dose indefinitely. If symptoms are not controlled on starting dosage, then escalate it. If the symptoms are not controlled by the first and second choice PPIs consider referral for specialist management.

Non-ulcer dyspepsia.

When symptoms are thought to be referable to the upper GI tract, but endoscopy is negative, the condition is described as non-ulcer dyspepsia. Other diagnoses such as gallstones, chronic pancreatitis or irritable bowel syndrome should be considered. Helicobacter pylori eradication will benefit a small proportion of these patients (need to treat 15 for 1 to benefit). In HP negative patients, or those in whom symptoms persist after eradication, a 1 month course of PPI or H2 receptor blocker can be offered. If symptoms improve on acid suppressing therapy and recur after its discontinuation, give the minimum dose to maintain symptomatic relief as maintenance therapy.

Acute upper gastrointestinal bleeding.

Both oral and intravenous PPI therapy reduce the risk of rebleeding and the need for surgery in patients with major peptic ulcer haemorrhage. They do not reduce the mortality rate. The intravenous route is likely to be the most reliable in an acutely bleeding patient. High dosage intravenous omeprazole should be given to patients identified at endoscopy to have a peptic ulcer with major stigma of recent haemorrhage (visible vessel or overlying clot), whether or not endoscopic therapy is given, or any patient with a peptic ulcer bleed and haemodynamic compromise (pulse rate greater than 100 per minute or systolic BP less than 100mm Hg).

Give omeprazole 80mg IV stat followed by a continuous infusion of 8mg per hour for 72 hours (80mg omeprazole in saline given over 10 hours is pharmacologically stable, see Appendix).

After completion of the high dosage regimen, give oral omeprazole 20mg per day.

There is no evidence to support the use of PPIs in undiagnosed acute upper GI bleeding but it is reasonable in a patient with major haemorrhage which may be due to peptic ulcer bleeding to commence high dosage omeprazole until the diagnosis is established.

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References

The NICE documents for referencing are:

1. Clinical guideline 14, issue date August 2004. Dyspepsia - management of dyspepsia in adults in primary care.
2. Clinical guideline 17, issue date June 2005. Referral guidelines for suspected cancer. Page 10 - Upper gastrointestinal cancer.

Appendix:

Administration of High Dose IV Omeprazole

Dose

Omeprazole 80mg IV over 1 hour followed by a continuous infusion of 8 mg per hour for 72 hours.

Preparation of infusion

Remove and discard 50ml from a 250ml sodium chloride 0.9% infusion bag.

Reconstitute 2 x 40mg vials by adding 5ml from the remaining 200ml infusion to each 40mg vial.

Add the reconstituted contents of the 2 x 40mg vials back into the infusion bag to give 80mg in 200ml sodium chloride 0.9%.

Administration

Omeprazole IV should only be administered as an IV infusion.

First dose

Administer the first 80mg dose over 1 hour.

Continuous infusion

Prepare 80mg in 200ml of sodium chloride 0.9% as above and infuse at 8mg per hour (20ml per hour) for 72 hours. An infusion bag will need to be prepared every 10 hours (x7) as there is no stability data available to extend the shelf life of the solution beyond 12 hours. The last bag will need to run for 2 hours (reconstitute 40mg in 100 mls sodium chloride 0.9%) and run for 2 hours discarding any remaining solution). An administration record sheet is available to record each infusion).

Stability

The reconstituted vials should be added to infusion fluid immediately after reconstitution. The prepared solution of 80mg in 200ml sodium chloride 0.9% is physically and chemically stable at 25 degrees C for 12 hours.

Possible side effects

Skin rashes, urticaria and pruritus which usually resolve on discontinuing treatment. Other GI effects include constipation, nausea/vomiting, flatulence and abdominal pain.

Omeprazole IV Infusion Administration Record Chart

(Please attach to infusion section of drug chart)

Patient Name: _____ Hospital no: _____

Ward: _____

Date	Time Start	Infusion Fluid/volume	Drug Added/dose	Duration	Batch number	Nurses initials	Time ended
		Sodium chloride 0.9% 200ml	Omeprazole 80mg	1 hour			
		Sodium chloride 0.9% 200ml	Omeprazole 80mg	10 hours			
		Sodium chloride 0.9% 200ml	Omeprazole 80mg	10 hours			
		Sodium chloride 0.9% 200ml	Omeprazole 80mg	10 hours			
		Sodium chloride 0.9% 200ml	Omeprazole 80mg	10 hours			
		Sodium chloride 0.9% 200ml	Omeprazole 80mg	10 hours			
		Sodium chloride 0.9% 200ml	Omeprazole 80mg	10 hours			
		Sodium chloride 0.9% 200ml	Omeprazole 80mg	10 hours			
		Sodium chloride 0.9% 200ml	Omeprazole 80mg	10 hours			
		Sodium chloride 0.9% 100ml	Omeprazole 40mg	Run at 20ml per hour for 2 hours and discard remainder			