Proton Pump Inhibitor (PPI) in Adults Guidance

NHS
Bath and North East Somerset, Swindon and Wiltshire
Clinical Commissioning Group

Background

- Diagnosis, referral and management should follow NICE CG184 2014 Management of dyspepsia in adults in primary care: https://www.nice.org.uk/guidance/cg184

On first presentation with dyspepsia symptoms:

- Review medications for possible causes of dyspepsia, for example, calcium antagonists, nitrates, theophyllines, bisphosphonates, steroids and non-steroidal anti-inflammatory drugs (NSAIDs).
- Consider trial of alginate or antacid if not already taking and review in one month if not needing referral.
- Patients undergoing endoscopy should be free from medication with a proton pump inhibitor (PPI) for a minimum of 2 weeks.
- If patient needs endoscopy stop NSAID and also where possible in un-investigated dyspepsia patients.

Lifestyle Measures – ALL PATIENTS SHOULD BE GIVEN THIS ADVICE

- Offer simple lifestyle advice, including advice on healthy eating, weight reduction and smoking cessation.
- Advise patients to avoid known precipitants they associate with their dyspepsia where possible. These may include smoking, alcohol, coffee, chocolate, fatty foods and being overweight.
- Raising the head of the bed (using bricks or a plank of wood, not by using more pillows) and having a main meal well before going to bed may help some people.
- Address psychosocial triggers, such as stress.
- Read codes for lifestyle advice should be recorded as follows:
  - Lifestyle counselling: 67H
  - Smoking cessation advice: 8CAL
  - Patient advised re diet: 8CA4
  - Alcohol advice: 8CAM
  - Advice re exercise: 8CA5

Risks Associated with PPIs

- Significant side effects are rare. Adverse effects are usually mild and reversible and include headache, diarrhoea, nausea, abdominal pain, constipation, dizziness and skin rashes.
- The association between the adverse effects listed below and long term use of PPIs is weak, but they are biologically plausible:
  - Clostridium difficile infection & other enteric infections
  - Increased risk of bone fractures
  - Acute interstitial nephritis
  - Increased mortality in older patients
  - Decreased iron absorption
  - Community acquired pneumonia
  - Hypomagnesaemia
  - Vitamin B12 deficiency
  - Rebound acid hypersecretion syndrome
  - Hyponatraemia
- Consider if benefits of PPI outweigh risks for patients susceptible to these conditions e.g. elderly, care home residents, respiratory patients, malnourished & immunocompromised patients. Review continuing need for treatment regularly.

Which PPI to use

- Prescribe low acquisition cost PPIs in preference to high acquisition cost PPIs, for the shortest duration (& clearly documented indications). There is no evidence that any PPI is more effective than another.
- **First-line PPIs:** Omeprazole or Lansoprazole CAPSULES.
- Both of these PPIs are also available as tablets but the tablets are 4-7 times more expensive.
- DO NOT prescribe by brand name which is approximately 13 times more expensive.

Patients with swallowing difficulties and with enteral feeding tubes

- Options are available which are dispersible (listed in increasing cost order):
  - Esomeprazole gastro-resistant **capsules** (caps can be opened and pellets mixed in non-carbonated water. The liquid can be drunk or administered through a gastric tube- see SPC).
  - Esomeprazole gastro-resistant **tablets** (tabs can be dispersed in non-carbonated water. The liquid can be drunk or administered through a gastric tube- see SPC).
  - Lansoprazole orodispersible tablets
  - Omeprazole dispersible gastro-resistant tablets

Omeprazole Powder for Oral Suspension (Rosemont) is NOT included on BSW formulary for use in adults. DO NOT PRESCRIBE.
Within BSW, this is RESTRICTED for use only following specialist recommendation for paediatric patients under 1 year of age or under 10kg whereby dispersible tabs/esomeprazole sachets are not appropriate (i.e. prescribed dose under 5mg or feeding tube in situ). Infants receiving doses ≥5mg or those with feeding tubes in situ at 12 months should transition to more cost effective PPI. See BSWformulary paediatric chapter

BSW CCG Medicines Optimisation Team Feb 2021 Bswccg.prescribing@nhs.net Minor update Feb 2021 to include updated information on omeprazole suspension and on esomeprazole granules and tablets.

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Dosage information on proton pump inhibitors (NICE CG184 2019)

Table 1: PPI doses relating to evidence synthesis and recommendations in the original CG17; 2004 guideline

PPI	Full/standard dose	Low dose (on-demand dose)	High/double dose
1. Omeprazole	20mg once a day	10mg once a day	40mg once a day
2. Lansoprazole	30mg once a day	15mg once a day	30mg[3] twice a day
3. Esomeprazole	20mg[1] once a day	Not available	40mg[2] once a day
Pantoprazole	40mg once a day	20mg once a day	40mg[3] twice a day
Rabeprazole	20mg once a day	10mg once a day	20mg[3] twice a day

1 Lower than the licensed starting dose for esomeprazole in Gastro-oesophageal Reflux Disease (GORD), which is 40mg, but considered to be dose-equivalent to other PPIs. When undertaking meta-analysis of dose related effects, NICE classed esomeprazole 20mg as a full-dose equivalent to omeprazole 20mg.

2 40mg is recommended as a double dose of esomeprazole because the 20-mg dose is considered equivalent to omeprazole 20mg.

3 Off-label dose for GORD.

NOTE: Pantoprazole and Rabeprazole are both NON-FORMULARY across BSWformulary.

Table 2: PPI doses for severe oesophagitis in the NICE CG184 2019 update

PPI	Full/standard dose	Low dose (on-demand dose)	High/double dose
1. Omeprazole	40mg[1] once a day	20mg[1] once a day	40mg[1] twice a day
2. Lansoprazole	30mg once a day	15mg once a day	30mg[2] twice a day
3. Esomeprazole	40mg[1] once a day	20mg[1] once a day	40mg[1] twice a day
Pantoprazole	40mg once a day	20mg once a day	40mg[2] twice a day
Rabeprazole	20mg once a day	10mg once a day	20mg[2] twice a day

1 Change from the 2004 dose, specifically for severe oesophagitis, agreed by the GDG during the update of CG17.

2 Off-label dose for GORD.

NOTE: Pantoprazole and Rabeprazole are both NON-FORMULARY across BSWformulary.

Patient Information and Review Timescales

- Ensure patients are aware of why they have been prescribed a PPI - supply patient leaflet from www.patient.co.uk
- Prescribe as acute for one month and ask patient to arrange a review appointment.
- Only put PPI on repeat if need for long-term therapy has been established.
- Explain to patients that over time their dose may be reduced and they may be asked to stop treatment once symptoms are well controlled.
- Some patients with GORD won't respond to a first-line PPI and so it is worth having a trial of a different PPI

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Prophylaxis of GI Complications due to concomitant medicines

Certain patient groups may need gastro-protection with PPIs during treatment with the following drugs:

NSAIDS

Gastro-protection should be given to:

• Anyone with osteoarthritis or rheumatoid arthritis (NICE)	• Concomitant oral steroids or anticoagulants
• Anyone ≥45 years of age with chronic low back pain (NICE)	• Requirement for prolonged use of maximal doses of NSAIDs
• Patients aged 65 and over	• Presence of cardiovascular disease, diabetes, hypertension, renal or hepatic impairment
• Past history of peptic ulcer disease (PUD) or serious GI complication	

Doses for NSAID Prophylaxis: Lansoprazole CAPSULES 15-30mg, Omeprazole CAPSULES 20mg

Note that people younger than 45 years of age and at low risk of GI adverse events (e.g. no history of GI bleeding or *Helicobacter pylori* infection and not on aspirin, warfarin, or oral corticosteroids) may not need the concomitant use of a gastro-protective drug with an NSAID.

If a patient develops GI symptoms after starting on an NSAID, stop the NSAID if possible to see if they resolve. If they don't resolve, further investigation is required.

ASPIRIN

Gastro-protect patients on low dose aspirin if also prescribed an NSAID, selective serotonin reuptake inhibitor (SSRI), or have a history of PUD or serious GI complication.

SSRIs

Gastro-protect patients on SSRIs if co-prescribed an NSAID. Consider/seek advice as to whether a different anti-depressant could be used to reduce the risk.

Review of patients taking PPIs

The following patient groups should be reviewed that are taking PPIs:

1.) Patients that can move from high dose to maintenance dose regimes

The following patients may be considered for step-down to the lowest maintenance dose of PPI (and change to generic, cost-effective PPI where applicable as per NICE), but should not proceed to self-management plans:

- Patients with a history of peptic ulceration associated with clo negative status.
- Patients diagnosed with Barrett's oesophagus (20mg maintenance dose omeprazole).
- Patients who must unavoidably continue with NSAID therapy apart from those considered at high risk i.e. those with previous ulceration; those on other medication harmful to the gastric and duodenal lining; the elderly and those on long term high NSAID use. (20mg Omeprazole is defined as maintenance dose for NSAID coverage).
- Patients using aspirin or clopidogrel to prevent cardiovascular disease can be stepped-off concomitant Proton Pump Inhibitor (PPI) treatment, apart from those considered to be at high risk e.g. those with previous ulceration; those on other medication harmful to the gastric or duodenal lining and the elderly.

To improve symptom control and the success of this dosage reduction, a suitable alginate/antacid symptomatic treatment may be recommended to prevent and/or treat occasional break through symptoms, due to rebound acid hypersecretion/acid breakthrough.

These patients can be reviewed for step off usually 2-3 months post step-down to maintenance dose.

2.) Patients that are on maintenance dose that can trial stopping their PPI

- Patients who have been prescribed a PPI maintenance dose for more than eight weeks and are not excluded by the specified exclusion criteria below should be counselled and recommended to be stepped off PPI treatment to a suitable alginate/antacid symptomatic treatment.
- Encourage patients to buy the alginate/antacid treatment themselves over the counter where possible.
- Ensure that patients understand that they should avoid long-term, frequent dose, continuous antacid therapy. It only relieves symptoms in the short term rather than preventing them.
- Some patients may need to use a PPI on a "PRN" basis for a short duration whilst stepping off treatment completely.
- Also consider stopping other medication which could be contributing to symptoms such as NSAIDs, SSRIs, anti-platelets, nitrates & nicorandil, bisphosphonates, corticosteroids and theophylline if appropriate to do so.

Follow up of these patients is not necessary but do encourage patients to report any further symptoms or issues.

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Review of patients taking PPIs: continued

3.) Patients that need to remain on a long-term PPI

Offer these patients an annual review of their condition and encourage them to try stepping down or stopping treatment (unless there is an underlying condition or co-medication that needs continuing treatment) when possible as & when their clinical circumstances allow.

Exclusion Criteria

The following patients are **not** suitable for PPI review:

- Patients on healing doses of PPIs <one month for un-investigated dyspepsia.
- Patients on maintenance dose PPIs <one month for non-ulcer dyspepsia.
- Patients on healing doses of PPIs <two months for gastro-oesophageal reflux disease/ peptic ulcer disease
- Patients currently on *H. Pylori* eradication therapy
- Patients under review at GI clinic or awaiting referral
- Patients awaiting gastroscopy or review
- Zollinger-Ellison Syndrome
- Patients at end stage in Gold Standard Framework
- Patients with grade 3 or 4 oesophagitis
- Patients on high dose steroids with life threatening or chronic illness, e.g. patients awaiting transplant, post-transplant patients
- Patients receiving immuno-suppression therapy
- Patients undergoing chemotherapy or radiotherapy
- Patients with oesophageal strictures or oesophageal dilation
- Patients with a history of oesophageal varices

Points for discussion with patient during review

- Is the prescribing for treatment or prophylaxis? If for prophylaxis, is the other drug still being prescribed or still needed?
- Check length of treatment and dosage - can healing dose be stepped down, maintenance dose stepped off?
- Check symptom control.
- Discuss risk factors associated with long term use of PPIs i.e. increased risk of fractures, pneumonia and *C. difficile*.
- Discuss lifestyle issues and read code for advice given.
- Discuss rebound effect and rescue treatment (alginate).
- Follow up after 2-3 months for patients moving down to a maintenance dose.

References

- NICE CG184 2019 Management of dyspepsia in adults in primary care: https://www.nice.org.uk/guidance/cg184