DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE (JAPC)

MANAGEMENT OF DYSPEPSIA AND GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD)

- Routine endoscopic investigation of patients of any age, presenting with dyspepsia and without ALARM signs, is not necessary. Alarm signs and signals are the major determinant of the need for endoscopy, not age on its own.

- Offer urgent direct access upper gastrointestinal endoscopy (to be performed within 2 weeks) to assess for oesophago-gastric cancer in people:
  - with dysphagia or
  - aged 55 and over with weight loss and any of the following:
    - ✓ upper abdominal pain
    - ✓ reflux
    - ✓ dyspepsia

- Consider non-urgent upper gastrointestinal endoscopy to assess for oesophago-gastric cancer in people with haematemesis.

- Consider non-urgent upper gastrointestinal endoscopy to assess for oesophago-gastric cancer in people aged 55 or over with:
  - treatment-resistant dyspepsia or
  - upper abdominal pain with low haemoglobin levels or
  - raised platelet count with any of the following:
    - ✓ nausea
    - ✓ vomiting
    - ✓ weight loss
    - ✓ reflux
    - ✓ dyspepsia
    - ✓ upper abdominal pain, or
  - nausea or vomiting with any of the following:
    - ✓ weight loss
    - ✓ reflux
    - ✓ upper abdominal pain

- For the management of un-investigated dyspepsia use clinical judgement to offer either *H pylori* "test-and-treat" or full dose PPI for one month. The stool antigen test is the preferred *H pylori* test across Derbyshire.

- Consider a referral to a specialist service for people of any age with gastro-oesophageal symptoms where *H pylori* that has not responded to second-line eradication therapy

- Patients should receive an annual review of their condition. Patients on a long-term PPI for GORD should be encouraged to either step-down to the lowest effective dose to control symptoms, continue treatment on a when needed bases or stop treatment

- Long-term use of PPIs is associated with adverse effects e.g. hip fractures, hypomagnesaemia and Clostridium difficile. See local PPI guideline.

Content

Introduction

Dyspepsia

The British Society of Gastroenterologists (BSG) defines dyspepsia as a group of symptoms that alert doctors to consider disease of the upper GI tract, and states that dyspepsia itself is not a diagnosis. These symptoms, which typically are present for 4 weeks or more, include upper abdominal pain or discomfort, heartburn, gastric reflux, nausea or vomiting.

Some of the costs associated with treating dyspepsia are decreasing, but the overall use of treatment is increasing. As a result, the management of dyspepsia continues to have potentially significant costs to the NHS.

Management of symptoms in primary care is appropriate for most patients rather than routinely seeking a pathological diagnosis. **Long-term care should emphasise patient empowerment, for example by promoting 'on demand' use of the lowest effective dose.**

Alarm signals and signs are the major determinant of the need for endoscopy, not age on its own.

Functional dyspepsia

Functional dyspepsia refers to patients whose endoscopic investigation has excluded gastric or duodenal ulcer, malignancy or oesophagitis.

Gastro-oesophageal reflux disease (GORD)

GORD is a chronic condition where gastric juices from the stomach (usually acidic) flow back up to the oesophagus. It can be severe or frequent enough to cause symptoms, or damage the oesophagus, or both. There are several risk factors for GORD including hiatus hernia, certain foods, heavy alcohol use, smoking, pregnancy.

Helicobacter pylori

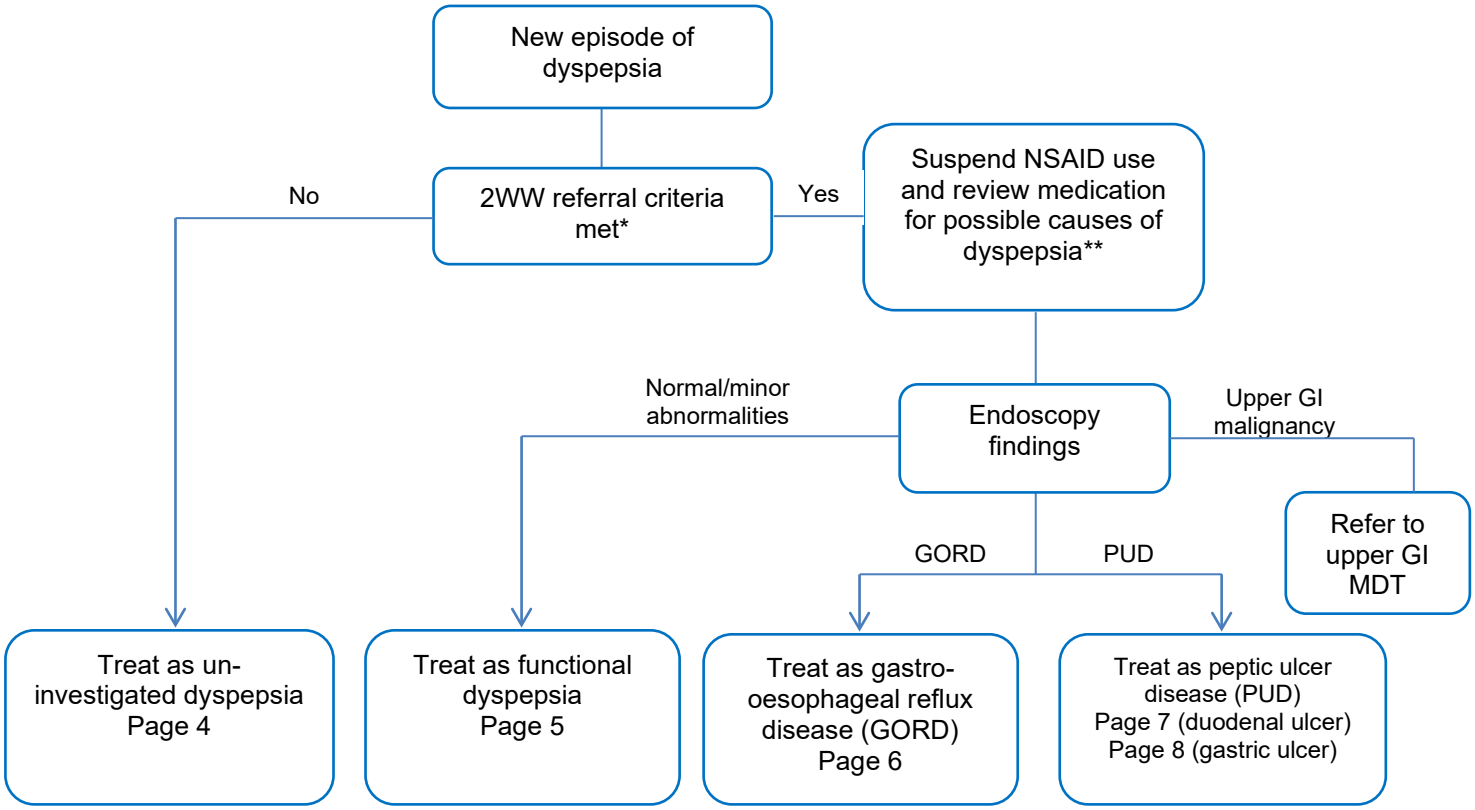
H pylori is widely present in the general population, often causing no harm, but is strongly associated with gastric and duodenal ulcers. The eradication of the bacterium is important in the management of peptic ulcer disease. *H pylori* infection may also be associated with functional dyspepsia, though its role in this condition is less clear. No causative association with GORD and oesophagitis has been demonstrated.

Test for *H pylori* using a stool antigen test. Near-patient *H pylori* serology tests cannot be recommended as they are not accurate enough.

Self-care

Include life-style changes (healthy eating, weight reduction, stop smoking) or using over the counter antacid and/or alginate therapy. However, long-term, frequent dose, continuous antacid therapy is not recommended.

Management of dyspepsia and GORD- overview



*__ALARM FEATURES REQUIRING REFERRAL VIA 2 WEEK WAIT SYSTEM__

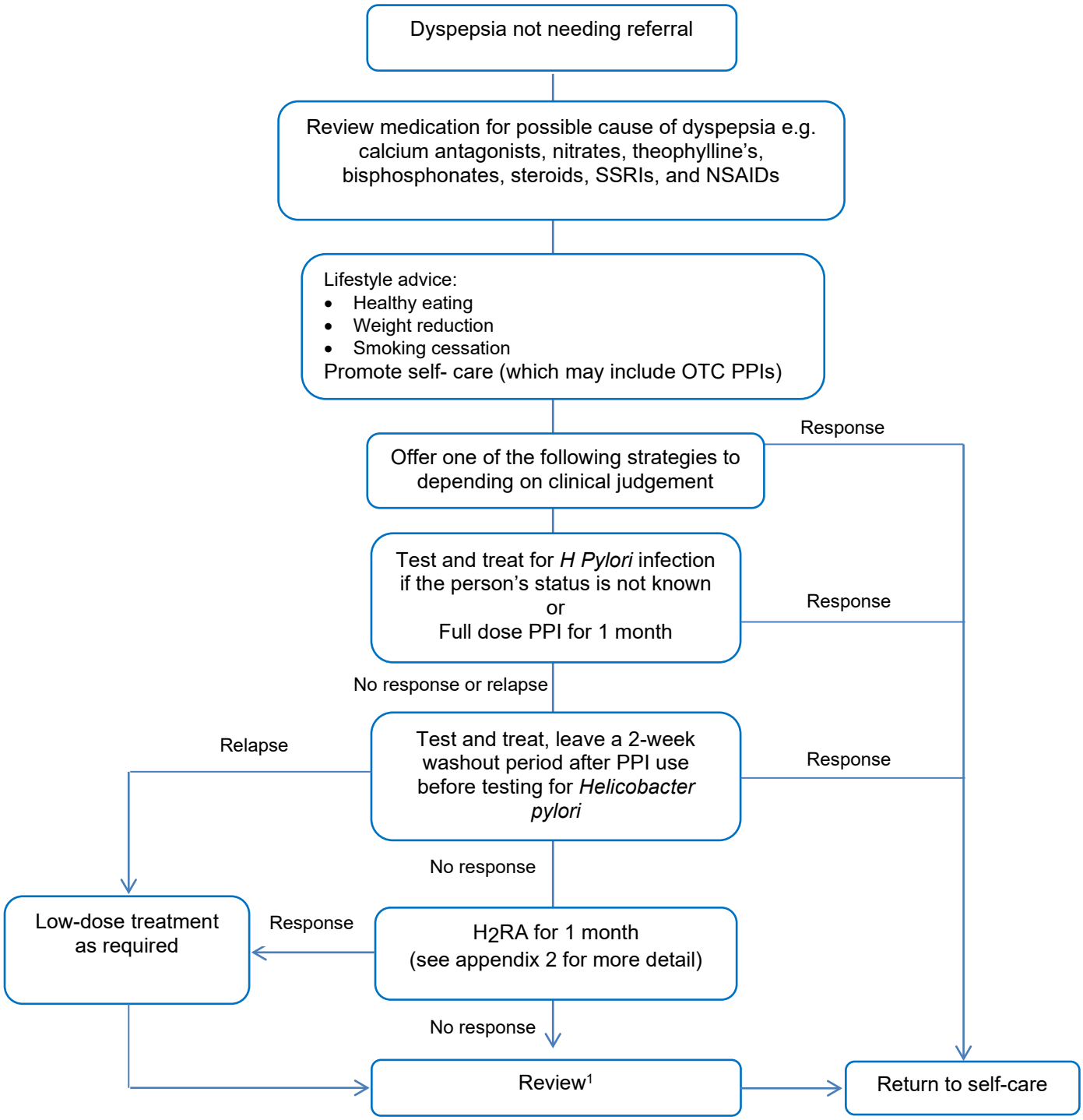
- Dysphagia or
- Aged 55 and over with weight loss and any of the following:
  - upper abdominal pain
  - reflux
  - dyspepsia
  - Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for people with an upper abdominal mass consistent with stomach cancer.

__Consider non urgent upper gastrointestinal endoscopy:__

- to assess for oesophago-gastric cancer in people with haematemesis
- to assess for oesophago-gastric cancer in people aged 55 or over with
  - treatment-resistant dyspepsia or
  - upper abdominal pain with low haemoglobin levels or
  - raised platelet count with any of the following:
    - ✓ nausea
    - ✓ vomiting
    - ✓ weight loss
    - ✓ reflux
    - ✓ dyspepsia
    - ✓ upper abdominal pain, or
  - nausea or vomiting with any of the following:
    - ✓ weight loss
    - ✓ reflux
    - ✓ dyspepsia
    - ✓ upper abdominal pain

** __Review medication for possible causes of dyspepsia e.g.:__
Calcium antagonists, nitrates, theophylline, bisphosphonates, steroids, NSAIDs and SSRIs

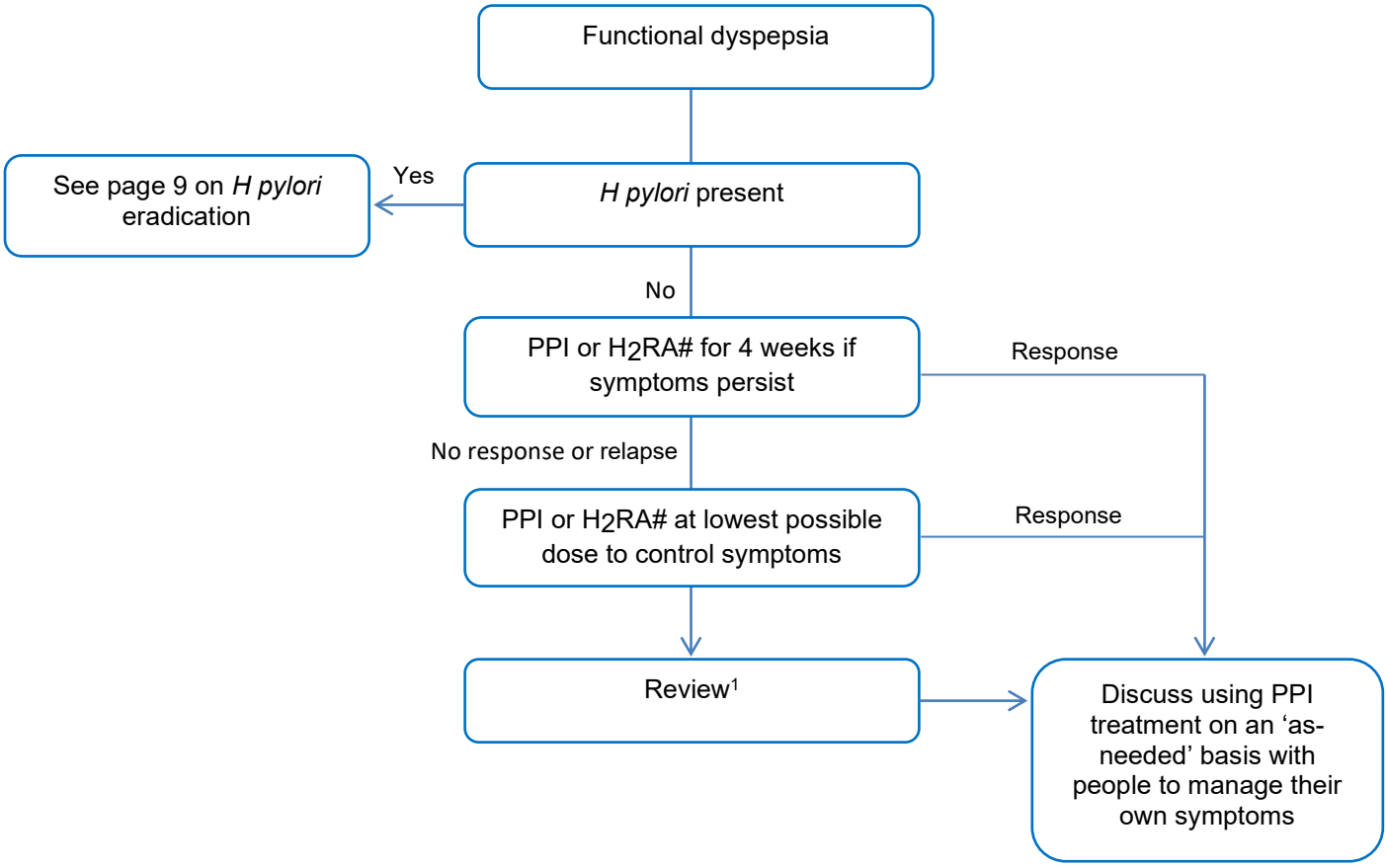
Interventions of un-investigated dyspepsia



[1] In some patients with an inadequate response to therapy it may become appropriate to refer to a specialist for a second opinion. Emphasise the benign nature of dyspepsia. Review long-term patient care at least annually to discuss medication and symptoms

For full and double doses of PPI see appendix 1

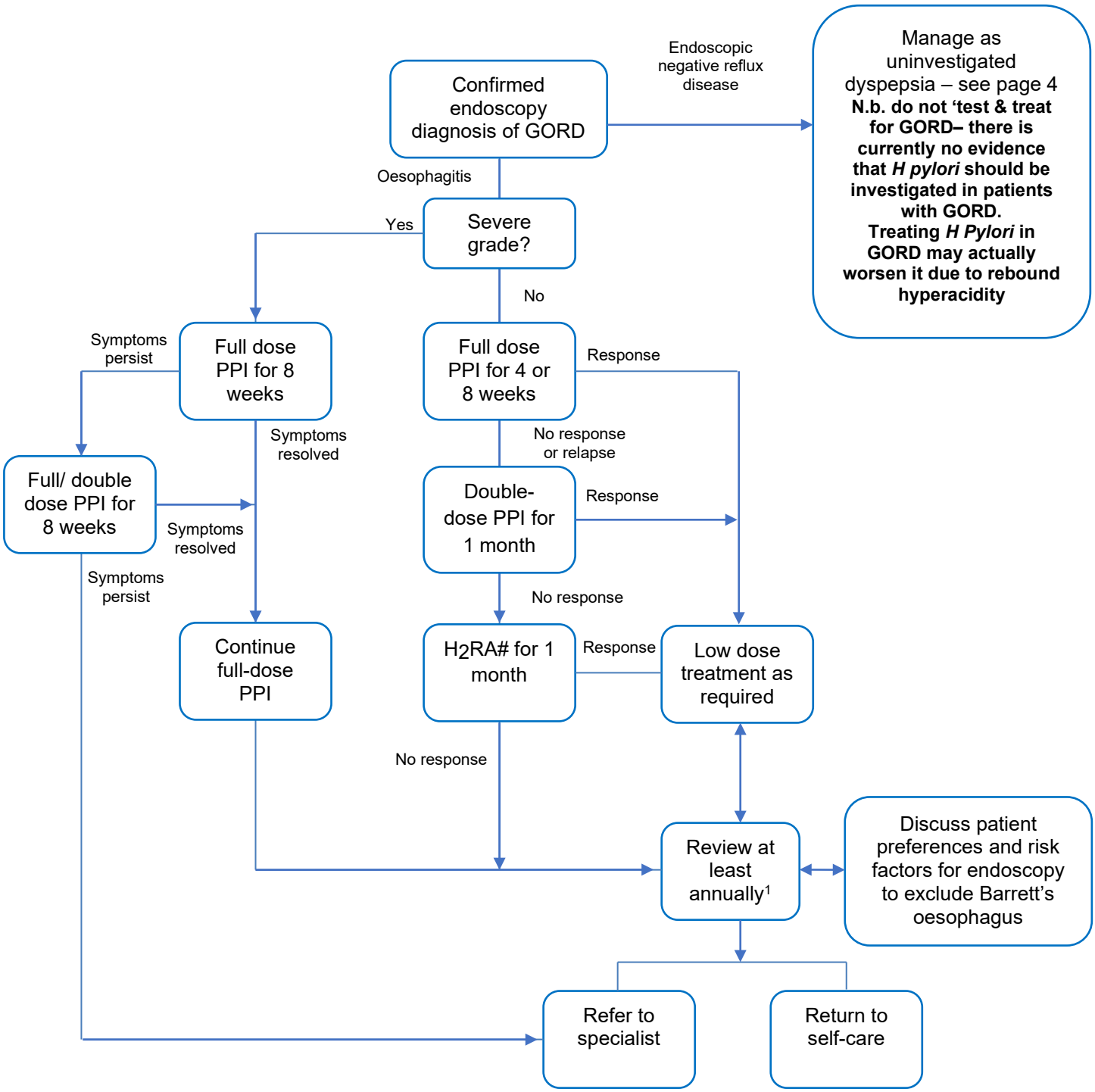
Management of functional dyspepsia



[1] In some patients with an inadequate response to therapy or new emergent symptoms it may become appropriate to refer to a specialist for a second opinion

see appendix 2 for more detail

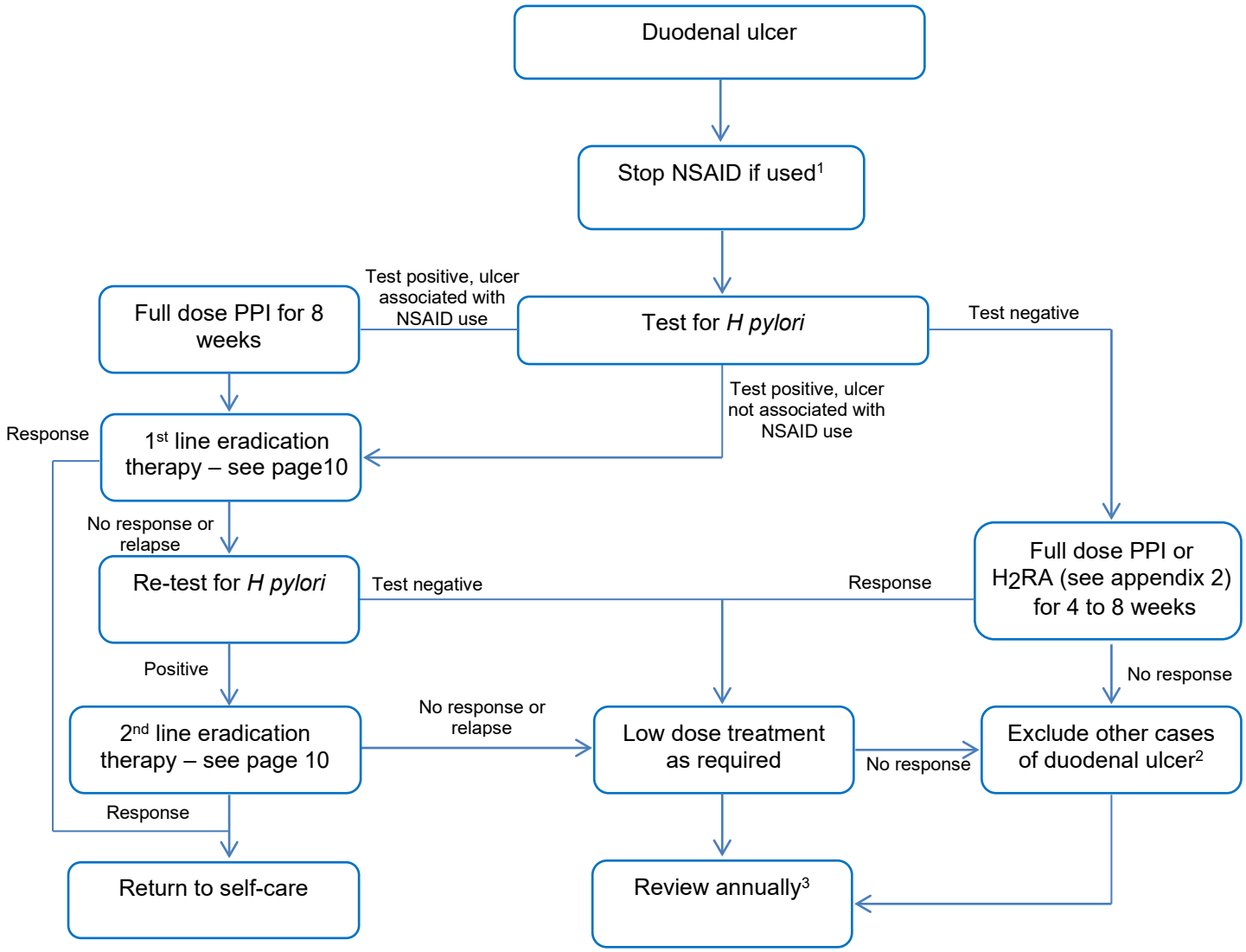
Management of gastro-oesophageal reflux disease (GORD) post endoscopy



[1] review long term patient care at least annually to discuss medication and symptoms. In some patients with an inadequate response to therapy or new emergent symptoms, it may be appropriate to refer to a specialist for a second opinion

see appendix 2 for more detail

Management of peptic ulcer disease post endoscopy- <u>Duodenal ulcer</u>



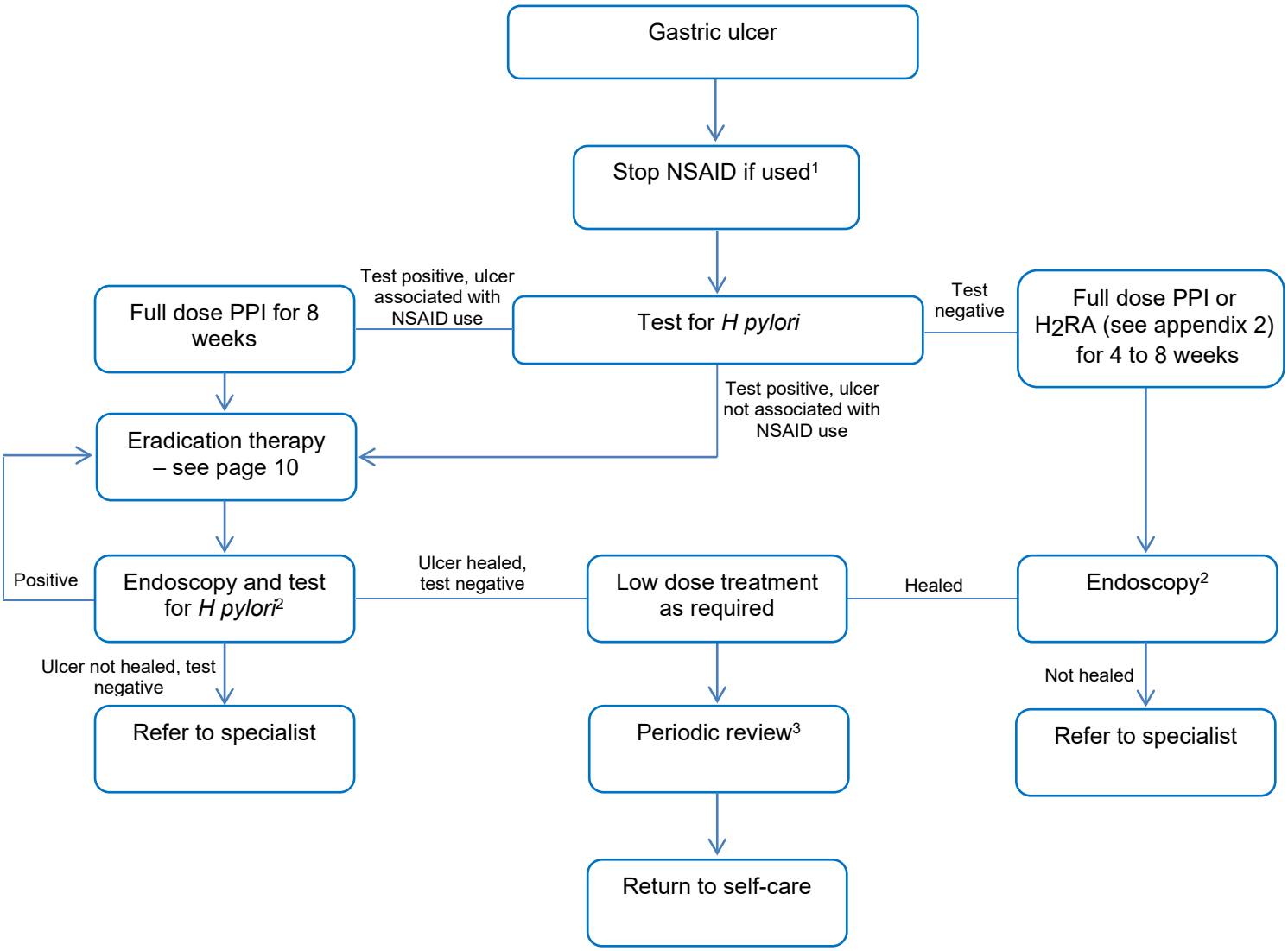
[1] If NSAID use is necessary, after ulcer healing offer long-term gastric protection

[2] Consider:

- Non-compliance with treatment
- Possible malignancy
- Failure to detect *H pylori* infection due to recent PPI or antibiotic use
- Inadequate testing
- Inadvertent use of aspirin or NSAID use
- Ulceration due to ingestion of other drugs
- Zollinger-Ellison syndrome
- Crohn's disease

[3] Review care annually, to discuss symptoms, promote stepwise withdrawal of therapy when appropriate and provide lifestyle advice

Management of peptic ulcer disease post endoscopy- Gastric ulcer



[1] If NSAID use is necessary, after ulcer healing offer long-term gastric protection
[2] Offer people with gastric ulcer and *H Pylori* repeat endoscopy 6 to 8 weeks after beginning treatment, depending on the size of the lesion
[3] Review care annually to discuss symptoms, promote stepwise withdrawal of therapy when appropriate and provide lifestyle advice. In some patients with an inadequate response to therapy it may become appropriate to refer to a specialist.

Management strategy for *Helicobacter pylori*

Advise the person to arrange a follow-up appointment if there are refractory or recurrent symptoms following initial management.

Asses or review for

- New alarm symptoms
- Alternative diagnosis
- Alternative antacids
- Reducing dose of NSAIDs if possible and or long term gastro-protection is necessary

If the person has received first-line *Helicobacter pylori* eradication therapy, do not routinely offer *H pylori* re-testing. Use clinical judgement considering:

- compliance to first-line eradication therapy
- whether the initial test was performed within 2 weeks of proton pump inhibitor (PPI) or within 4 weeks of antibiotic therapy
- family history of gastric malignancy
- if patient has severe, persistent, or recurrent symptoms.

If *H pylori* re-testing is indicated, arrange this at least four weeks (ideally 8 weeks) after initial eradication therapy (if this was needed)

Consider referral from primary care if there are refractory or recurrent symptoms despite optimal management in primary care.

- If endoscopy is planned, ensure the person stops any acid suppression therapy for at least 2 weeks before the procedure date, and suggest self-treatment with antacid and/or alginate therapy if needed.
- Treatment with a second-line *H pylori* eradication regimen has been unsuccessful

Testing

The H pylori stool antigen test can be used both for diagnosis and post-eradication confirmation (if this is appropriate). If the patient is taking PPIs or bismuth, then a period of 2 weeks treatment free should elapse before testing or false negatives may occur. If the patient is taking antibiotics, leave a period of 4 weeks treatment free period before testing.

To request a test, send a stool sample with a standard microbiology request form asking for *H pylori* antigen test and stating whether for diagnosis or eradication confirmation.

Treatment – *H pylori* eradication regimens (as recommended by NICE CG 184)

All courses are for <u>7 days</u> unless stated otherwise.

If the ulcer is large or complicated by haemorrhage or perforation then the PPI should be continued for at least another 3 weeks.

Choose the treatment regimen with the lowest acquisition cost, and take into account previous exposure to clarithromycin or metronidazole	
1st line	Lansoprazole 30mg BD **or** omeprazole 20mg-40mg BD Amoxicillin 1gram BD Either clarithromycin 500mg BD **or** metronidazole 400mg BD
1st line, allergic to penicillin	Lansoprazole 30mg BD **or** omeprazole 20mg-40mg BD Clarithromycin 500mg BD Metronidazole 400mg BD

Offer 2nd line treatment to people who still have symptoms after 1st line eradication treatment	
2nd line	Lansoprazole 30mg BD **or** omeprazole 20mg-40mg BD Amoxicillin 1gram BD Either clarithromycin 500mg BD or metronidazole 400mg BD (whichever was not used first line)
2nd line, allergic to penicillin, no previous exposure to a quinolone	Lansoprazole 30mg BD **or** omeprazole 20mg-40mg BD Metronidazole 400mg BD Levofloxacin 250mg BD (unlicensed)
2nd line, previous exposure to metronidazole and clarithromycin:	Lansoprazole 30mg BD **or** omeprazole 20mg-40mg BD Amoxicillin 1gram BD either tetracycline OR levofloxacin (if tetracycline not tolerated)

Seek advice or consider referral to a specialist service if eradication of *H pylori* is not successful with second-line treatment

Reviewing patient care

Patients who need long-term management of dyspepsia symptoms should be offered an annual review of their condition. Patients should be encouraged to step down or stop treatment. It may be appropriate to advise patients to return to self-treatment with antacid and/or alginate therapy.

References

- NICE clinical guideline 184: Dyspepsia and gastro-oesophageal reflux disease, September 2014
- www.guidelines.co.uk/nice_dyspepsia_2014 – Dyspepsia and gastro-oesophageal reflux disease (accessed: November 2014; August 2019)
- Suspected cancer: recognition and referral NICE guideline Published: 23 June 2015 NICE guidelines [NG12]
- PHE Helicobacter pylori: quick reference guide. Accessed August 2019 via https://www.gov.uk/government/publications/helicobacter-pylori-diagnosis-and-treatment#history

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Document control	Date

Appendix 1 – Dosage information on PPIs

Table 1 – PPI doses

Proton pump inhibitor	Full/standard dose	Low dose (on-demand dose)	Double dose
Lansoprazole	30mg once a day	15mg once a day	30mg[1] twice a day
Omeprazole	20mg once a day	10mg[1] once a day	40mg once a day
Pantoprazole	40mg once a day	20mg once a day	40mg1 twice a day
[1] Off-label dose for GORD			

Table 2 – PPI doses for severe oesophagitis

Proton pump inhibitor	Full/standard dose	Low dose (on-demand dose)	Double dose
Lansoprazole	30mg once a day	15mg once a day	30mg[2] twice a day
Omeprazole	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
[1] NICE CG184 updated dosing specifically for sever oesophagitis [2] Off-label dose for GORD			

Appendix 2 Ranitidine/ H2 receptor antagonist shortage

JAPC has classified ranitidine **GREY** (May 2020) as per EMA's human medicines committee (CHMP) recommendation to suspend all ranitidine medicines in the EU due to the presence of low levels of an impurity N-nitrosodimethylamine (NDMA).

Existing patients prescribed oral ranitidine should be reviewed to establish if ongoing treatment is still required, and to consider switching to an PPI where clinically appropriate. If a PPI was unsuitable then an alternative H2RA may be considered.

There are ongoing supply disruptions for ranitidine and all other H2RAs. JAPC advises the types of patients who may require an alternative H2RA to ranitidine include:

1. those needing acid suppression who are genuinely allergic or intolerant or contraindicated to all PPIs, which is rare;
2. those needing acid suppression where low magnesium occurs, which is felt as very rare;
3. those who have needed upward titration for reflux symptoms despite high dose PPIs, where addition of H2RA, generally at night time, helps*.
4. occasionally there seems to be a small number who claim not to do well on PPI yet symptomatically get better on H2RA.

** Patients suitable for antireflux procedures should be referred at this point, but generally the H2RA+PPI combination is used for those not suitable for or who would not do well with antireflux surgery (e.g. elderly frail, or those where there is a functional element to symptoms). Patient may be advised to go back to PPI+ antacid.*

For all cases, those not responding well to PPIs should be investigated to make sure diagnosis correct e.g. to rule out bile reflux, functional pain etc. No particular problems should arise with stopping H2RA as the rebound hyper acid phase tends not to occur (compared to PPIs).

Alternative H2RA cost table (Drug Tariff, September 2022)

Drug	**Standard dose**	**Monthly cost (30 days)**
Cimetidine**	400mg twice a day	£26.05
Nizatidine	150 twice a day	£30.20
Famotidine	20mg twice a day	£34.33

Consider indication/ need for H2RA as per JAPC advise above. H2RAs cost significantly more than PPIs. Check caution e.g. renal impairment and interactions. e.g. azol antifungals, protease inhibitors.

**CKS does not recommend cimetidine for treatment of GORD as there is a higher risk of drug interactions, due to inhibition of cytochrome P450 enzymes.