

Management of **Dyspepsia** and **Heartburn**

**Evidence-based
Best Practice
Guideline
SUMMARY**

JUNE 2004

KEY MESSAGES

Initial Evaluation

- Identify risk factors for organic pathology. If there are alarm signals, or if age >50 years at first presentation, refer for oesophago-gastro-duodenoscopy (OGD).
- If there is any heartburn, manage as GORD.
- If a NSAID is being used, evaluate risk of GI complications, as well as potential benefit (eg, from aspirin use for prevention of cardiovascular events and stroke).

Undifferentiated Dyspepsia

- If prevalence of *H. pylori* >30%, treat empirically (domperidone or H₂RA for 4 – 12 weeks) **OR** test for *H. pylori* and treat if positive. If there is no response to test-and-treat, or if prevalence of *H. pylori* <30%, treat empirically. If there is no response to either strategy, refer for OGD.

GORD

- Commence empiric step-down therapy, and adjust according to response.
- If there is no response or early recurrence after cessation of treatment, refer for OGD, and manage according to the severity (Grade) of GORD.

H. pylori Management

- Test for *H. pylori* in those with past history of peptic ulcer, family history of gastric cancer, or where the prevalence of *H. pylori* is >30%. Urea breath test is recommended. Serology can be used where the prevalence of *H. pylori* is >30%. Faecal antigen test is also recommended, and is becoming increasingly available in New Zealand. If testing is positive, treat with triple therapy.
- Check eradication of *H. pylori* in those with a peptic ulcer complication, important comorbidity factors, symptom recurrence or those living in isolated areas. Re-treat if testing is positive.

Peptic Ulcer

- If peptic ulcer is identified, test for *H. pylori*, treat if positive, and start a PPI or H₂RA. Treat gastric ulcers for 8 – 12 weeks, and check healing with OGD. Treat duodenal ulcers for 4 – 8 weeks (not essential if *H. pylori* eradicated and no complications).

NSAID Use

- If there is no dyspepsia, consider a safer alternative, or a less toxic NSAID (eg, ibuprofen). If continued use is required, and there is increased risk of GI complications, consider a PPI or misoprostol, or possibly a COX-2 inhibitor (providing patient not on aspirin).
- If there is dyspepsia and increased risk of GI complications, refer for OGD. Eradicate *H. pylori* if positive at OGD.
- If there is dyspepsia and no increase in risk, stop NSAID, use a safer alternative, reduce the dose, or use a less toxic NSAID. If symptoms continue, refer for OGD. Eradicate *H. pylori* if positive at OGD.
- If an ulcer is identified, and continued NSAID use is required, treat with a PPI, and consider use of a COX-2 inhibitor as an alternative.

This Guideline is endorsed by:



Supported by: Royal Australasian College of Surgeons – New Zealand Branch
The Royal New Zealand College of General Practitioners

This evidence-based, best practice guideline provides recommendations for diagnosis, evaluation and treatment of dyspepsia, GORD, peptic ulcer and management of *H. pylori*.

1. DYSPEPSIA AND/OR HEARTBURN: INITIAL EVALUATION

- If there are any alarm signals, or if the person is aged >50 years at first presentation, refer for OGD. **(B)**
- If the diagnosis is in doubt and the patient continues to have troublesome symptoms, refer for OGD.
- If there is any heartburn, manage as GORD. **(A)**
 - 75% of those with heartburn have GORD.
- If there is concurrent use of NSAIDs, evaluate for risk of GI complications, and consider alternative strategies if risk is increased.
 - NSAIDs are associated with significant mortality and morbidity, particularly in older people, those who are frail, and those with previous upper GI pathology: their use should be avoided or minimised wherever possible.
- If there are none of the above, manage according to the prevalence of *H. pylori* infection (see Undifferentiated Dyspepsia); if the prevalence is >30%, treat empirically (domperidone or H₂RA for 4 – 12 weeks) **OR** test for *H. pylori* and treat if positive. If there is no response to test-and-treat, or if prevalence of *H. pylori* <30%, treat empirically.
 - *H. pylori* eradication is effective in healing peptic ulcers, and also very significantly reduces ulcer recurrence (rare) and complications.
 - Blind testing of all dyspeptic individuals or treating them empirically for *H. pylori* without testing is not recommended. A test-and-treat strategy for *H. pylori* has been shown to be safe and to reduce the number and cost of OGDs when applied to dyspeptic individuals aged <50 years with no alarm signals in areas of moderate to high *H. pylori* prevalence (>30%).

Grades of Recommendation

- A** Requires at least one RCT as part of the body of literature of overall good quality and consistency addressing specific recommendation
- B** Requires availability of well-conducted studies but no RCTs addressing specific recommendation
- C** Requires evidence obtained from expert committee reports or opinions, and/or clinical experiences of respected authorities
- Indicates absence of directly applicable clinical studies of good quality

Details of the grading system are available in the full guideline at www.nzgg.org.nz

Abbreviations

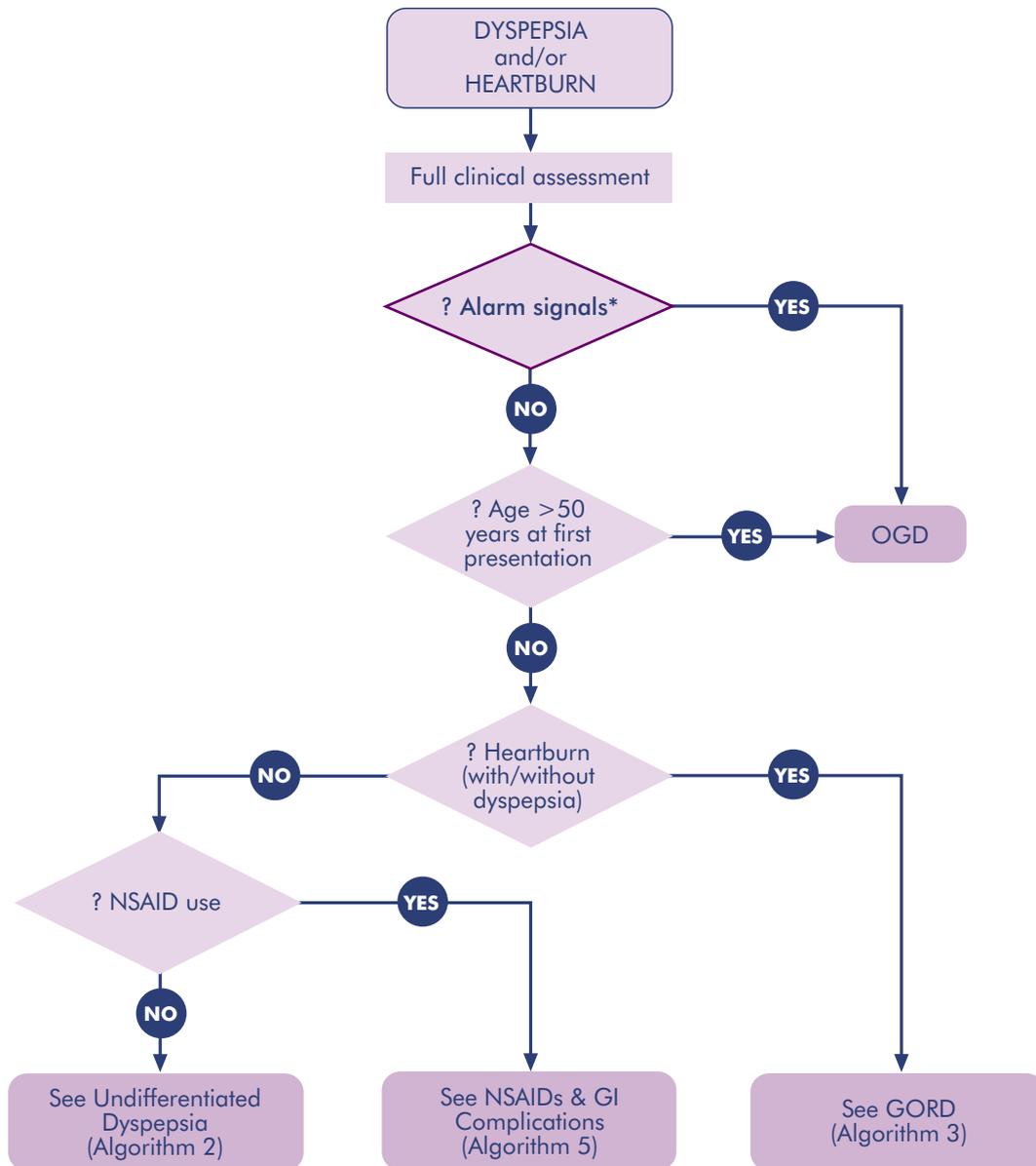
COX-2	Cyclo-oxygenase-2 inhibitor
GI	Gastro-intestinal
GORD	Gastro-oesophageal reflux disease
<i>H. pylori</i>	<i>Helicobacter pylori</i>
H ₂ RA	Histamine type 2 receptor antagonist
NNT	Number needed to treat
NSAID	Non-steroidal anti-inflammatory drug
OGD	Oesophago-gastro-duodenoscopy
PPI	Proton pump inhibitor
RCT	Randomised controlled trial
UBT	Urea breath test

This guideline was developed by the core committee of the Dyspepsia and GORD Working Party: Gil Barbezat (Chair), Philip Bagshaw, Kristin Good, Owen Lloyd, Andrew Orange, Ann Richardson, and Don Simmers. Regional committee members included: Richard Milne, Ralf Lubcke, Brendan O’Neill, Ross Roberts, Larry Skiba, Tim Cookson, Vint Chadwick, Anthony Dowell, Rob McIlroy, Marilyn Tucker, Erica Amon, Chris Cochrane, John Petrie, David Shaw, Andrea Steinberg and Ian Wallace.

The guideline has been funded by PHARMAC, AstraZeneca, Janssen-Cilag, the National Health Committee, the Ministry of Health and the NZGG.

ALGORITHM 1

DYSPEPSIA and/or HEARTBURN: Initial Evaluation



*Alarm Signals

People with alarm signals must be referred for OGD investigation. Alarm signals, which increase the likelihood of significant organic disease, include the following:

- family history of gastric cancer (onset <50 years)
- severe or persistent dyspeptic symptoms
- previous peptic ulcer disease, particularly if complicated
- ingestion of NSAIDs in those at risk (see Algorithm 5: NSAID and GI Complications)
- unexplained weight loss

- gastrointestinal bleeding (haematemesis or melaena)
- anaemia
- dysphagia (difficulty swallowing)
- coughing spells or nocturnal aspiration
- protracted vomiting or persistent regurgitation of food
- palpable abdominal mass.

NB: All symptoms should be regarded as more serious in people who are aged >50 years when presenting for the first time. Gastric cancer tends to occur a decade earlier in people of Maori, Pacific Island or Asian origin.

2. UNDIFFERENTIATED DYSPEPSIA

OVERVIEW

- This section applies to those with no alarm signals, age <50 years at first presentation, no NSAID use, and no heartburn (see Algorithm 1: Dyspepsia and/or Heartburn: Initial Evaluation).
- Treatment responses of those with dyspepsia differ from those with heartburn (75% of whom have GORD). People with heartburn respond best to PPIs, while those with undifferentiated dyspepsia respond better to prokinetic agents and H₂RAs.
- The test-and-treat strategy for *H. pylori* infection has been shown to be effective in areas of moderate to high (>30%) *H. pylori* prevalence. There is no evidence of efficacy for this strategy in areas of low *H. pylori* prevalence.
- If there is no pathology identified with OGD, manage as Functional Dyspepsia.

INITIAL MANAGEMENT

- If there is dyspepsia but no heartburn (reflux) symptoms, either:
 - treat initially with domperidone or an H₂RA **(A) OR**
 - test for *H. pylori* and treat if positive, if age <50 years and prevalence of *H. pylori* >30%.**(A)**
- Review lifestyle factors (eg, diet, weight, smoking, alcohol).

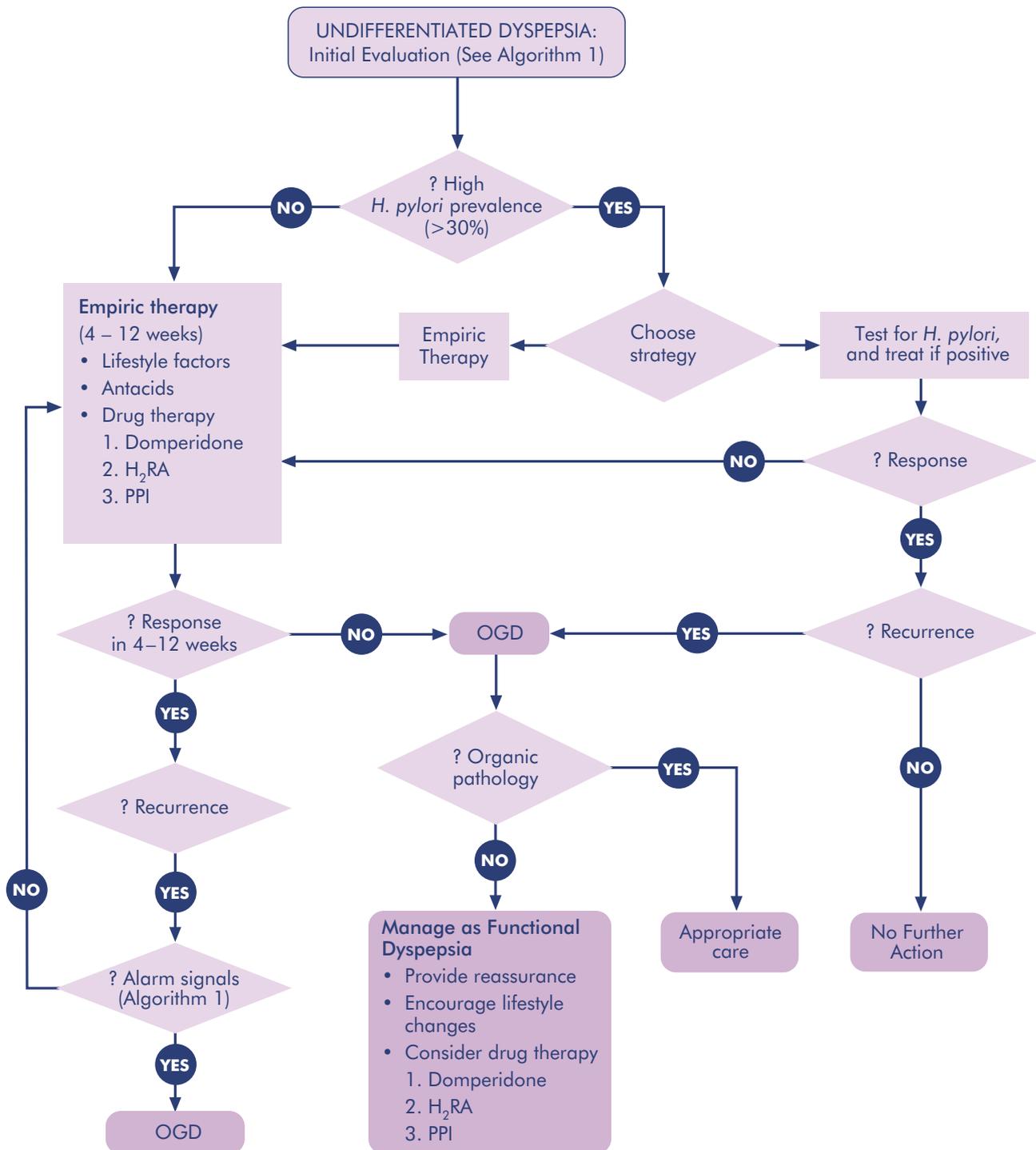
MANAGEMENT OF RECURRING UNDIFFERENTIATED DYSPEPSIA

- If there is failure to respond to treatment in 4 – 12 weeks, refer for OGD. **(C)**
- If previous dyspepsia symptoms recur 1 – 6 months after cessation of treatment, re-evaluate for alarm signals. **(C)**
- If previous dyspepsia symptoms recur after 6 months, with no alarm signals, repeat empiric therapy. **(C)**
- Consider *H. pylori* eradication. **(A)**
 - Benefit is variable.

MANAGEMENT OF FUNCTIONAL DYSPEPSIA

- Provide reassurance regarding the absence of organic pathology. **(C)**
- Encourage lifestyle changes: diet, weight control, smoking cessation, and alcohol moderation. **(C)**
- Consider drug therapy in the following order: **(A)**
 1. domperidone; NNT 2.8 (NNT based on total prokinetics studied)
 2. H₂RA; NNT=5.9
 3. PPI; NNT=11.1.
- Consider *H. pylori* eradication. **(A)**
 - Benefit is variable.
- Check patient:
 - does not have heartburn, and is not taking NSAIDs
 - has normal blood tests (FBC, ESR, CRP)
 - has normal OGD.

ALGORITHM 2 UNDIFFERENTIATED DYSPEPSIA



Although data regarding the prevalence of *H. pylori* infection in New Zealand are patchy, the following statements can be made:

- rates in the South Island are well below 30%
- rates tend to be >30% in adult Maori, Pacific peoples, native populations in Asia, and those with lower socio-economic status
- rates in adults living in Auckland have generally been found to be >30%.

3. GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD)

OVERVIEW

- This section applies to those with heartburn, age <50 years at first presentation, and no alarm signals (see Algorithm 1; Dyspepsia and/or Heartburn: Initial Evaluation).
- Severity of symptoms does not necessarily correlate with endoscopic findings as approximately 50% of people with heartburn have no endoscopic evidence of inflammation (Grade O).
- Symptomatic response and healing are more rapid and complete with PPIs than with H₂RAs.
- PPIs and H₂RAs given to relieve heartburn, can mask signs of inflammation at OGD. When referring for OGD, symptoms can be relieved with antacids or alginates for at least one month prior to the procedure.

GORD SYMPTOMS

- Consider GORD in people with:
 - heartburn (burning sensation radiating from the epigastrium towards the neck) **(A)**
 - non-cardiac chest pain, asthma, chronic cough, hoarseness of voice and erosion of teeth. **(B)**

INITIAL MANAGEMENT WITH EMPIRIC THERAPY

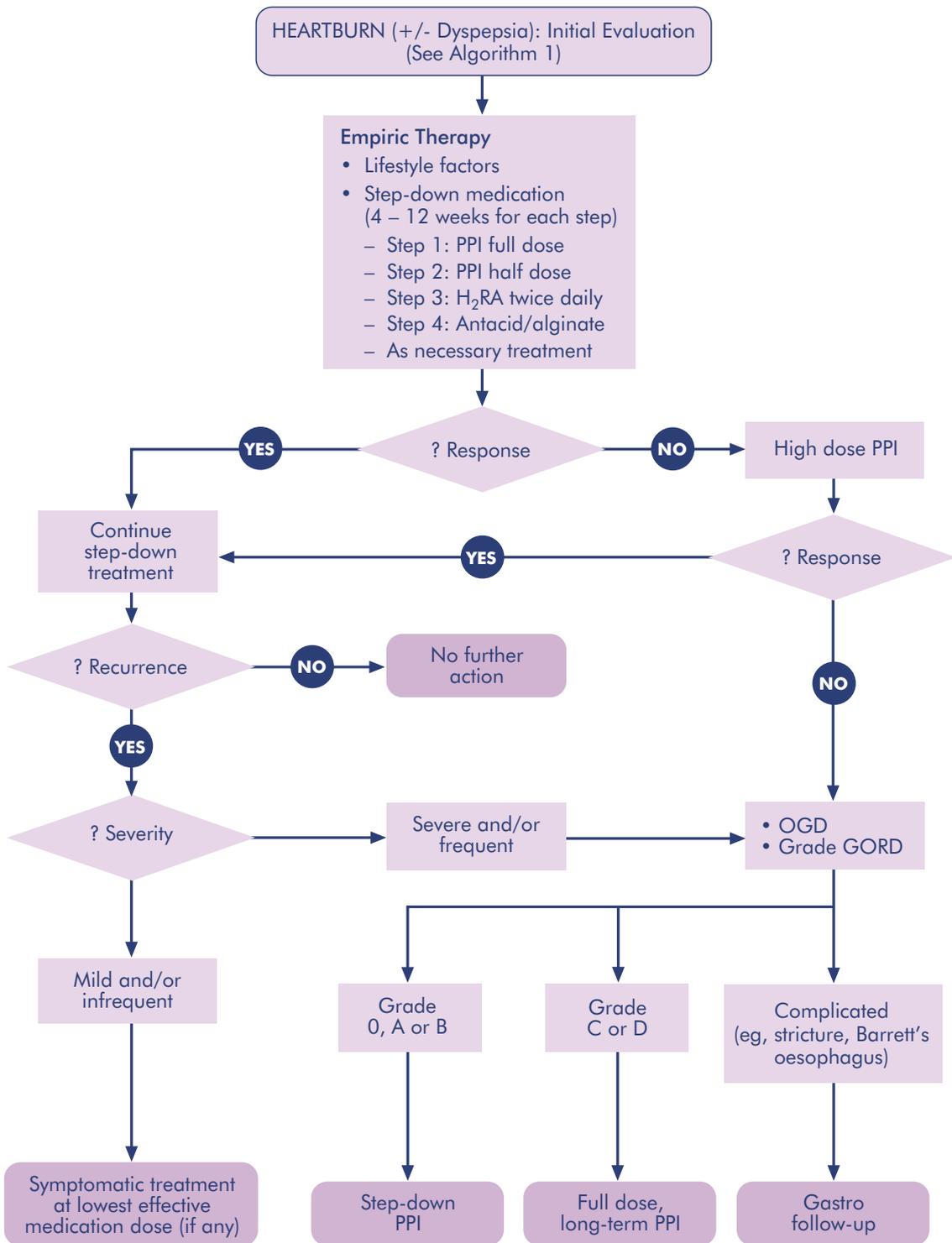
- If the person's symptoms are suggestive of GORD, treat with a step-down drug regimen, usually in 4 – 8 week steps: **(A)**
 - Step 1. full-dose PPI (omeprazole 20 mg, lansoprazole 30 mg, pantoprazole 40 mg) daily
 - Step 2. half-dose PPI
 - Step 3. H₂RA (famotidine 20 – 40 mg, ranitidine 150 – 300 mg) twice daily
 - Step 4. antacids/alginate.

- If there is no response to full dose PPI therapy, double the dose. **(B)**
- Continue treatment for at least 3 – 6 months. **(B)**
- If the person fails to respond, or if symptoms recur within 1 month after end of treatment, consider OGD rather than long-term empiric therapy. **(B)**

TREATMENT OF GORD DIAGNOSED AFTER OGD

- People with grades 0, A and B **(A)**
 - Treat with a step-down drug regimen (see Algorithm 3: Heartburn +/- Dyspepsia: Empiric Therapy).
 - If symptoms recur at stepped-down dosage, continue on lowest effective dose; intermittent therapy may control symptoms.
- People with grades C and D **(A)**
 - Treat with ongoing continuous full-dose PPI treatment.
- Consider surgery as an alternative to long-term drug treatment if:
 - age <50 years
 - age 50 years and over and there is no comorbidity
 - there is inability or unwillingness to take medications
 - there is inadequate control with medical therapy.
- If high-dose PPI treatment fails, re-evaluate symptoms and consider 24-hour pH telemetry. **(B)**
- In people with Barrett's oesophagus or unresolved complications (grade D), re-evaluate with OGD if necessary. **(B)**

ALGORITHM 3 GORD



Note: Surgery is an alternative for selected people

4. H. PYLORI AND PEPTIC ULCERATION

INITIAL DIAGNOSTIC INVESTIGATION FOR H. PYLORI

- Test for *H. pylori* in those:
 - who originate from areas of high (>30%) *H. pylori* prevalence **(A)**
 - with present or past history of peptic ulcer **(A)**
 - with Mucosa-associated lymphoid tissue lymphoma **(B)**
 - with a family history of gastric cancer. **(C)**
- Recommended diagnostic tests
 - UBT is the recommended non-invasive test. Stop treatment (other than antacids) for 2 weeks prior to UBT. **(A)**
 - Although UBT and faecal antigen tests are also valid options, serology (validated with sensitivity and specificity of at least 90%) is recommended where the prevalence of *H. pylori* is high (>30%). **(A)**
 - Faecal antigen test is also recommended, and is becoming increasingly available in New Zealand. Omeprazole can interfere with the result. **(A)**
 - If OGD is being performed for investigation of dyspepsia, consider testing with the rapid urea test, histology or culture. **(B)**

INITIAL TREATMENT OF H. PYLORI

- Give triple therapy: regimens containing PPI, clarithromycin, and amoxicillin or metronidazole, have consistently high eradication rates after one week. **(A)**
- Substitute metronidazole for amoxicillin in penicillin-allergic individuals. **(A)**
- Emphasise to the person that successful eradication depends on compliance with treatment regimen. **(B)**

H. PYLORI TREATMENT FAILURE

- For initial treatment failure, use either of the following for 1 week: **(A)**
 - an alternative triple therapy regimen (PPI plus two of the following: clarithromycin, amoxicillin, metronidazole, tinidazole, tetracycline and bismuth), OR
 - quadruple therapy (standard triple therapy plus bismuth).

- For repeated treatment failure:
 - review compliance factors and consider testing for bacterial resistance **(B)**
 - consider retreatment for 2 weeks. **(C)**

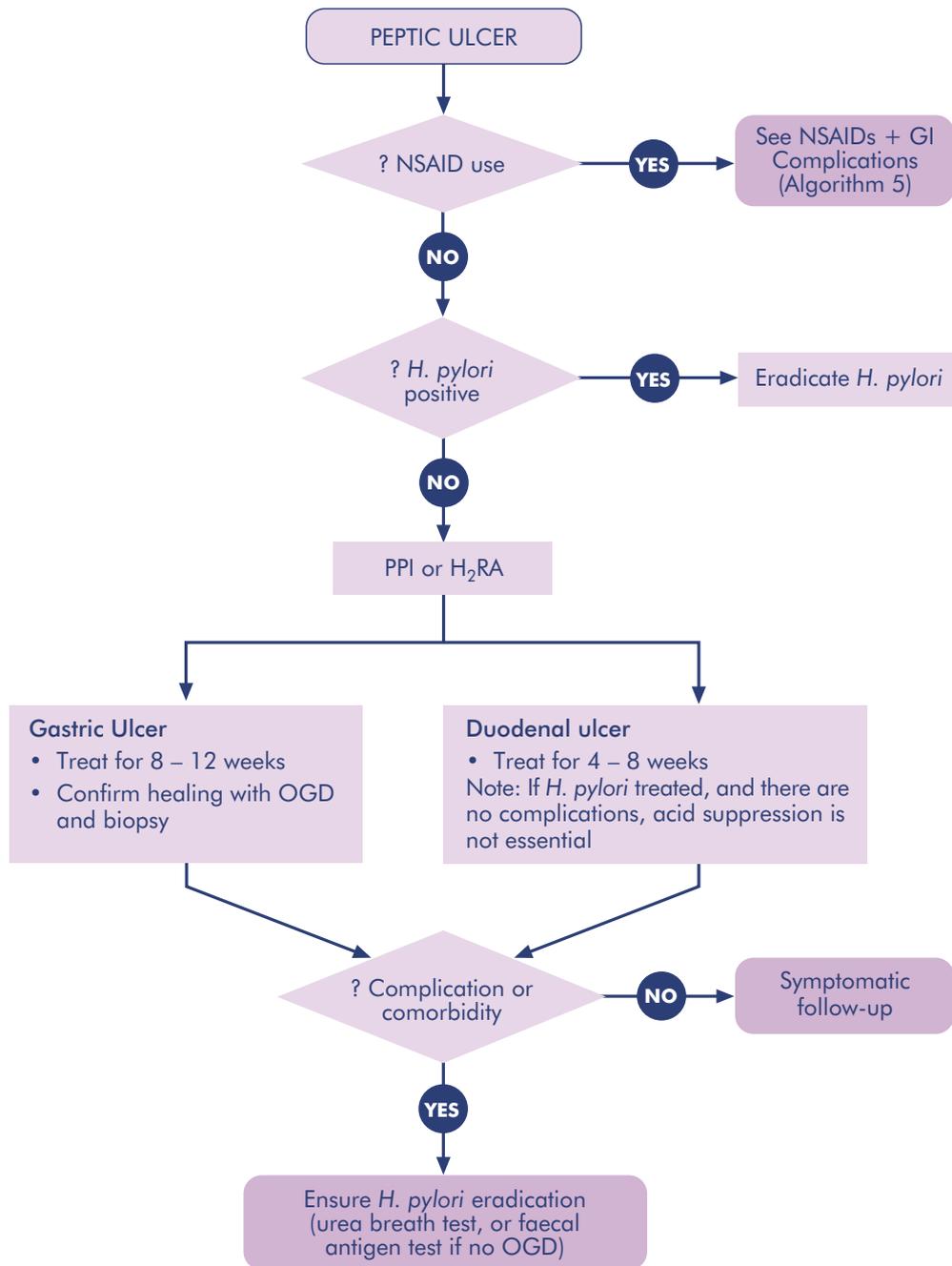
CONFIRMATION OF H. PYLORI ERADICATION

- Confirm eradication of *H. pylori* in those with a peptic ulcer complication, important comorbidity factors, symptom recurrence or residence in isolated areas. **(B)**
- Recommended tests
 - UBT is the recommended non-invasive test (*serology should not be used because it takes 6 – 12 months to become negative*). **(B)**
 - *H. pylori* stool antigen may be used for confirmation of eradication at least 4 weeks after stopping treatment. Omeprazole can interfere with result. **(A)**
 - For people having OGD to check for healing of gastric ulcer, confirm eradication by histology. **(C)**
- Timing of tests
 - Perform at least one month after completion of eradication regimen. **(B)**
 - For people taking PPIs, perform at least one week after cessation of PPI. **(C)**

MANAGEMENT OF H. PYLORI-NEGATIVE PEPTIC ULCERS

- Treat duodenal ulcers with H₂RAs or PPIs for 4 – 8 weeks. **(A)**
- Treat gastric ulcers with PPIs or H₂RAs for 8 – 12 weeks and confirm healing with OGD. **(A)**
- Use maintenance treatment with H₂RA or PPI if: **(C)**
 - ulcer recurrences are frequent (eg, more than once per 12 months) or severe
 - there is a previous peptic ulcer complication
 - there are comorbid factors that might make any complications life-threatening.

ALGORITHM 4 PEPTIC ULCER



5. NSAIDS AND GI COMPLICATIONS

OVERVIEW

- GI intolerance to NSAID is a systemic effect which occurs whether the drug is taken orally, parenterally or rectally.
- NSAID-related complications (haemorrhage, ulceration, perforation) can occur in otherwise asymptomatic individuals.
- Low-dose aspirin produces significant inhibition of gastric mucosal prostaglandins even when taken as an enteric coated tablet.
- Although COX-2 selective agents have less GI adverse effects than other NSAIDs, total withdrawals from drug trials because of all adverse effects are similar to non-selective NSAIDs.
- COX-2 selective agents lose their specificity when prescribed with aspirin.

INCREASED RISK OF NSAID-INDUCED GI COMPLICATIONS

- Begin treatment with either of the following: **(A)**
 - misoprostol at doses of 200 mcg/day. Increase dose over two weeks as tolerated, to a maximal dose of 800 mcg/day
 - standard doses of PPI once daily.
- Eradicate *H. pylori*, if testing is positive. **(A)**

TREATMENT OF NSAID-RELATED DYSPEPSIA

- Review person's history for risk factors. **(C)**
- Stop NSAID if possible. **(C)**
- In person with symptoms and risk factors, refer for OGD. **(C)**
- If ongoing symptom relief is needed:
 - continue NSAID with co-prescription of PPI or misoprostol **(A)** OR
 - replace NSAID with COX-2 selective inhibitor. **(B)**
- Eradicate *H. pylori* if testing is positive. **(A)**

MANAGEMENT OF NSAID-INDUCED PEPTIC ULCER

- If NSAID can be stopped, treat with an H₂RA (ranitidine 150 mg twice daily or famotidine 20 mg twice daily) or PPI (omeprazole 20 mg, lansoprazole 30 mg or pantoprazole 40 mg) for 8 weeks for duodenal ulcers and 12 weeks for gastric ulcers. **(A)**
- If NSAID needed:
 - treat with PPI for 8 weeks for duodenal ulcer and 12 weeks for gastric ulcer; if unsuccessful increase dose. Ongoing maintenance treatment is advised (as for individuals at increased risk of NSAID-induced GI complications) (Grade A)
 - consider replacement of NSAID with COX-2 selective inhibitor. **(C)**
- Eradicate *H. pylori* if testing is positive. **(A)**
- Refer individuals with complications (ie, bleeding, perforations, obstruction) to specialist. **(C)**
- Check healing of gastric ulcer with OGD. **(C)**

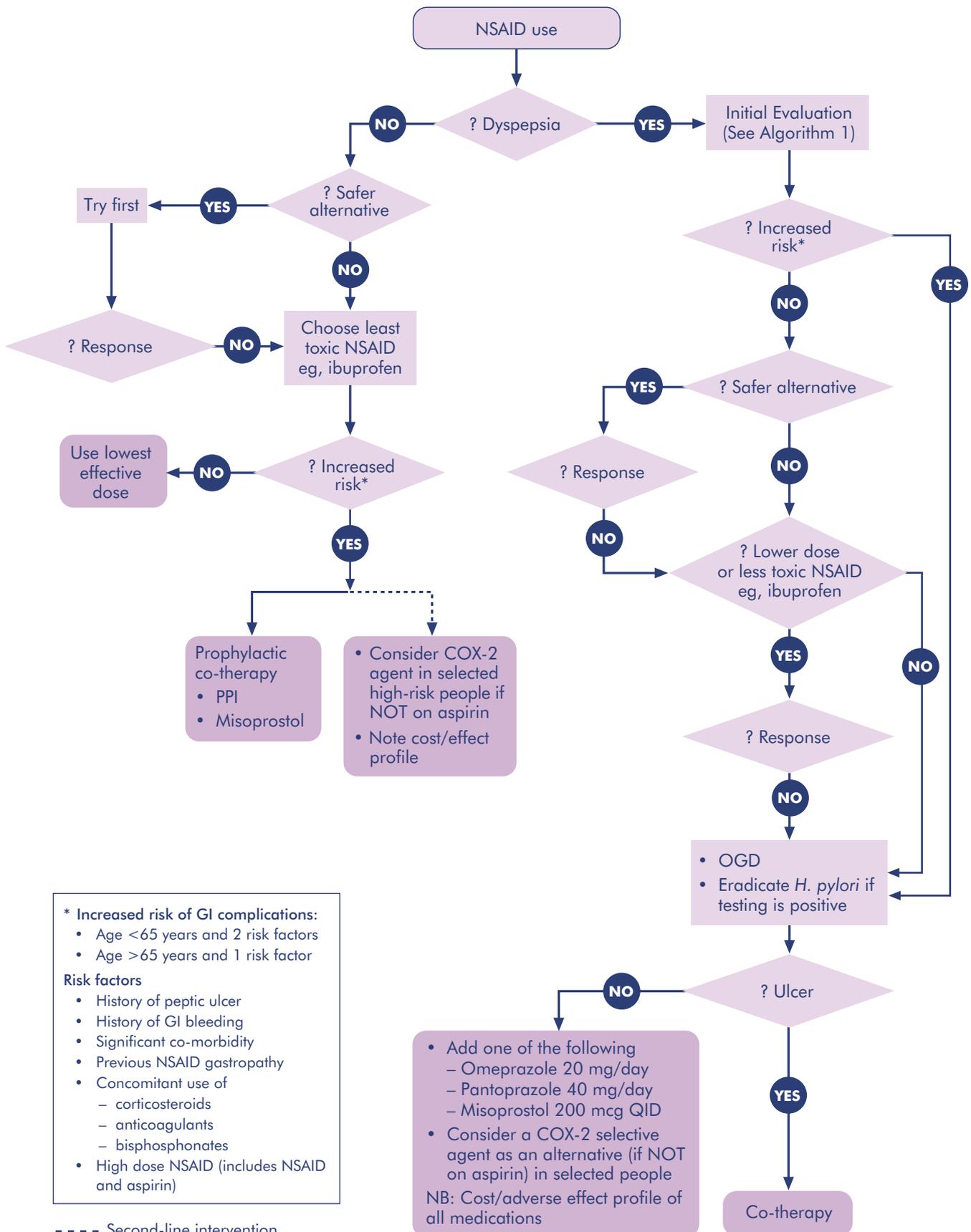
GI toxicity of NSAIDs (ibuprofen as reference)

Comparator	Pooled RR	95% CI for pooled RR
Ibuprofen	1.0	-
Fenoprofen	1.6	1.0 – 2.5
Aspirin	1.6	1.3 – 2.0
Diclofenac	1.8	1.4 – 2.3
Sulindac	2.1	1.6 – 2.7
Diflunisal	2.2	1.2 – 4.1
Naproxen	2.2	1.7 – 2.9
Indomethacin	2.4	1.9 – 3.1
Piroxicam	3.8	2.7 – 5.2
Ketoprofen	3.8	2.7 – 6.4
Azapropazone	9.2	4.0 – 21.0

Note: Doses used were those prescribed in the 12 studies using 14 drugs assessed in this meta-analysis

Source: Henry D, Lim LLY, Rodriguez LAG, et al. Variability in risk of GI complications with individual NSAIDs: results of a collaborative meta-analysis. *BMJ* 1996; 312:1563–6.

ALGORITHM 5 NSAIDS AND GI COMPLICATIONS



*** Increased risk of GI complications:**

- Age <65 years and 2 risk factors
- Age >65 years and 1 risk factor

Risk factors

- History of peptic ulcer
- History of GI bleeding
- Significant co-morbidity
- Previous NSAID gastropathy
- Concomitant use of
 - corticosteroids
 - anticoagulants
 - bisphosphonates
- High dose NSAID (includes NSAID and aspirin)

- - - - Second-line intervention

RECOMMENDED MEDICATION FOR HEARTBURN AND/OR DYSPEPSIA

Antacids/alginate may be used for symptomatic control. Doses will vary.

Proton pump inhibitors

	Half dose	Standard dose	Double dose
Lansoprazole	15 mg/day	30 mg/day	60 mg/day OR 30 mg BD
Omeprazole	10 mg/day	20 mg/day	40 mg/day OR 20 mg BD
Pantoprazole	20 mg/day	40 mg/day	80 mg/day OR 40 mg BD

H₂-receptor antagonists

	Peptic ulcer		GORD	
	Treatment	Maintenance	Treatment	Maintenance
Famotidine	40 mg nocte OR 20 mg BD	20 mg nocte	40 mg BD	20 mg BD
Ranitidine	300 mg nocte OR 150 mg BD	150 – 300 mg nocte	150 – 300 mg BD	150 mg BD

Prokinetic agents

Domperidone	10 mg 3 – 4 times daily	Dose can be increased (to double) after 2 weeks
Metoclopramide	10 mg TDS	Metoclopramide is less favoured: <ul style="list-style-type: none"> • potential extrapyramidal adverse effects • no eligible studies were found to support its use.

H. pylori eradication therapy

Initial therapy		
Triple therapy (7 days)	Option 1	<ul style="list-style-type: none"> • PPI (standard dose) BD • Clarithromycin 500 mg BD • Amoxicillin 1000 mg BD
	Option 2 (penicillin allergy)	<ul style="list-style-type: none"> • PPI (standard dose) BD • Clarithromycin 500 mg BD • Metronidazole 400 mg BD
Initial treatment failure		
Triple therapy (7 days)		<ul style="list-style-type: none"> • PPI (standard dose) BD PLUS 2 of the following: <ul style="list-style-type: none"> – Clarithromycin 500 mg BD – Amoxicillin 1000 mg BD – Metronidazole 400 mg BD – Tinidazole 500 mg BD – Tetracycline 500 mg QID – Colloidal bismuth 120 mg QID.
Repeated treatment failure		
Quadruple therapy (7 days)	Option 1	<ul style="list-style-type: none"> • PPI (standard dose) BD • Clarithromycin 500 mg BD • Amoxicillin 1000 mg BD • Colloidal bismuth 120 mg QID
	Option 2	<ul style="list-style-type: none"> • PPI (standard dose) BD • Clarithromycin 500 mg BD • Metronidazole 400 mg BD • Colloidal bismuth 120 mg QID
	Option 3	<ul style="list-style-type: none"> • PPI (standard dose) BD • Tetracycline 500 mg QID • Metronidazole 400 mg BD • Colloidal bismuth 120 mg QID
<p>Note: Some advocate treatment for 14 days for repeated treatment failure</p>		

June 2004

This guideline was developed by the NZGG.

An electronic copy of the full guideline is available for download from www.nzgg.org.nz or a printed copy is available from info@nzgg.org.nz, phone 64-4-471 4180 or Box 10-665, Wellington, New Zealand.