KEY MESSAGES

Proton pump inhibitor (PPI) use remains high in Wales and continues to increase at around 7% per year: there is therefore a need to tackle inappropriate prescribing and/or overprescribing.

Safety concerns relating to PPIs mean that prescribers should only use PPIs in patients for whom there is clear benefit; safety concerns relating to PPIs include rebound hypersecretion, osteoporotic fractures, tubulointerstitial nephritis, hypomagnesaemia, cancer, *Clostridium difficile*, and community- and hospital-acquired pneumonia.

Prescribers should attempt to manage dyspepsia whilst minimising PPI overuse via the following:

- Stop medicines which may exacerbate dyspepsia where possible: non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, calcium antagonists, theophyllines, bisphosphonates, iron, slow-release potassium, nitrates and anticholinergic drugs.

- Provide patients with appropriate lifestyle advice: lose weight, stop smoking, reduce alcohol and caffeine intake, and avoid food/drink that worsens dyspeptic symptoms.

- Test and treat for *Helicobacter pylori* where appropriate.

- Step up: use “as required” or use regular alginate first and consider prescribing PPIs for short courses where needed, and step down: use lowest dose of PPI possible or consider “as required” PPI therapy.

- When discontinuing long-term (> 8 weeks) PPIs, reduce dose and use concomitant alginate cover to prevent rebound hypersecretion.

- Prescribe low acquisition cost PPIs in preference to high acquisition cost PPIs: there is no evidence that any one PPI is more effective than another.

- Ensure clear documentation in patient records: indication for treatment, lifestyle and self-management advice, management plan and review date, reason for high dose/high acquisition cost PPI.
## CONTENTS

1.0 AIMS .......................................................................................................................... 3

2.0 INTRODUCTION ........................................................................................................ 3

3.0 DYSPEPSIA ................................................................................................................ 4

3.1 Definitions .................................................................................................................. 4

3.2 Prevalence .................................................................................................................. 4

3.3 Symptoms .................................................................................................................. 4

3.4 Causes ....................................................................................................................... 4

3.5 Endoscopy .................................................................................................................. 5

3.6 Managing dyspepsia ................................................................................................... 6

3.6.1 Clinical history and physical examination ......................................................... 6

3.6.2 Lifestyle advice .................................................................................................... 6

3.6.3 Drug treatment ..................................................................................................... 7

3.6.4 *H. pylori* testing and eradication ....................................................................... 7

3.6.5 Community pharmacist support in managing patients with dyspepsia ............... 8

4.0 PROTON PUMP INHIBITORS .................................................................................. 9

4.1 PPI prescribing ......................................................................................................... 9

4.2 Safety of long-term PPI use ..................................................................................... 9

4.2.1 Rebound hypersecretion ..................................................................................... 10

4.2.2 Osteoporotic fractures ....................................................................................... 10

4.2.3 Tubulo-interstitial nephritis ............................................................................... 10

4.2.4 Hypomagnesaemia ............................................................................................ 10

4.2.5 Cancer ................................................................................................................ 11

4.2.6 Clostridium difficile ........................................................................................... 11

4.2.7 Community- and hospital-acquired pneumonia ................................................ 11

4.3 Choice of PPI ........................................................................................................... 11

4.4 PPI review ................................................................................................................. 12

4.5 General prescribing points ...................................................................................... 13

REFERENCES ................................................................................................................ 14

APPENDIX 1: MANAGEMENT OF DYSPEPSIA ......................................................... 16

APPENDIX 2: PPI REVIEW: MAIN ACTION POINTS ............................................. 17

APPENDIX 3: PPI REVIEW TOOLKIT ......................................................................... 18

APPENDIX 4: PPI PATIENT INFORMATION LEAFLET (ENGLISH AND WELSH) ..... 21

APPENDIX 5: INDIVIDUAL DATA COLLECTION FORM FOR PPI REVIEW .......... 23

APPENDIX 6: GP PRACTICE SUMMARY FORM ......................................................... 25

Developed by the Welsh Analytical Prescribing Support Unit (WAPSU) for the All Wales Therapeutics and Toxicology Centre (AWTTC) as part of the Invest to Save (ITS) initiative 2011–2012.
1.0 AIMS

This resource pack aims to:

- identify the role of proton pump inhibitors (PPIs) in the management of dyspepsia;
- support the appropriate prescribing of PPIs across Wales;
- provide a quality improvement toolkit to assist in the review and discontinuation of PPIs where appropriate.

2.0 INTRODUCTION

PPIs are licensed for the short-term treatment of a number of conditions including peptic ulcer disease (PUD), dyspepsia, eradication of Helicobacter pylori and gastro-oesophageal reflux disease (GORD)\(^1\). Following completion of the course, the PPI should be reviewed and, if appropriate, discontinued. Longer term courses may be required for control of excessive acid secretion in patients with Zollinger–Ellison syndrome, and prevention and treatment of NSAID-associated ulcers.

PPI use is continuing to rise, increasing by around 7% per year across Wales, as shown by the prescribing trend in Figure 1. This trend is similar whether PPI use is measured as prescriptions dispensed, total quantity of PPIs dispensed or defined daily doses dispensed.

A possible explanation for this rapid and continuous increase in use is that they are often used in patients for whom they were never indicated, as there is no clear evidence of acid symptoms, or they are continued despite no longer being indicated\(^2\). Reduced concerns regarding the potential side-effects of PPIs, and the reduction in cost as more agents become available generically, is leading to their more liberal use\(^3\).

As a consequence, PPIs are being used in patients for a variety of gastrointestinal complaints that are not known to be acid-induced\(^4\). The percentage of patients now receiving long-term PPI treatment is higher than the prevalence of the diseases that are commonly accepted as the appropriate indications for their use\(^5\). Studies suggest that between 25% and 70% of patients being prescribed PPIs have no true indication for treatment\(^4\).

Figure 1. PPI primary care prescribing trend in Wales – June 2004–December 2012
Welsh Analytical Prescribing Support Unit

The National Institute for Health and Care Excellence (NICE) published its technology appraisal ‘Dyspepsia – Proton Pump Inhibitors’ in July 2000; this was subsequently updated as a clinical guideline in August 2004\(^1\). Its recommendations for using these drugs – particularly in the long term – are relatively selective. If prescriptions were restricted to the recommended indications, expenditure on PPIs would be far less than 90% of the total dyspepsia drug budget\(^4\). Therefore, it can be assumed that these guidelines are not being followed.

PPIs are generally well tolerated; the incidence of short-term adverse events is low. However, there is some evidence that both long-term and high-dose use of PPIs are associated with an increased risk of fractures of the hip, wrist, and spine, and increase the risk of *Clostridium difficile* infection, and hospital- and community-acquired pneumonia.

Acid suppression with PPIs has been shown to result in rebound hypersecretion during treatment discontinuation, even after only eight weeks of treatment. Rebound hypersecretion could present as a worsening of symptoms that could be mistaken for disease relapse and may lead to patients being re-initiated on a PPI.

### 3.0 DYSPEPSIA

#### 3.1 Definitions

Dyspepsia means “bad digestion” and the term is used to describe a range of symptoms, although it has no universally accepted definition. Dyspepsia represents a complex of symptoms, not a diagnosis, and can be broadly described as any symptom of the upper gastrointestinal tract, present for four weeks or more\(^1\).

#### 3.2 Prevalence

Annually, 40% of the adult population will have symptoms of dyspepsia, with about 5% consulting their GP\(^1\). About 1% of the population will be referred for endoscopy each year\(^1\).

#### 3.3 Symptoms

Symptoms of dyspepsia include upper abdominal discomfort, retrosternal pain, anorexia, nausea, vomiting, bloating, fullness, early satiety and heartburn. These symptoms amongst others should alert doctors to consider disease of the upper gastrointestinal tract.

#### 3.4 Causes

Dyspeptic symptoms can have several organic causes, but in many cases no obvious cause is identified (functional dyspepsia)\(^5\).

Where endoscopy is performed, differentiation is possible between GORD (oesophagitis or endoscopically negative reflux disease), PUD including gastric and duodenal ulcer disease, functional or “non-ulcer” dyspepsia (NUD) and cancer\(^1\). Of those undergoing endoscopy, 20% have oesophagitis, 13% have PUD and 1.4% have Barrett's oesophagus (defined as columnar-lined oesophageal mucosa)\(^1\). Only 3% have gastric/oesophageal cancer. Up to 60% have functional dyspepsia or NUD, where endoscopic investigation has excluded gastric or duodenal ulcers, malignancy and oesophagitis, and no causal pathology or disease is identified\(^1\).

It is possible with a good clinical history to diagnose both GORD and functional dyspepsia without endoscopy in younger patients.

Dyspepsia-related symptoms can also be caused by: cholelithiasis and cholecystitis, pancreatitis and pancreatic cancer, hepatobiliary disorders and malignancy, ischaemic heart disease and certain medications. The main medicines which can cause
dyspepsia are shown in Table 1. Where possible these medicines should be reviewed and either discontinued or, if it is not clinically appropriate to discontinue and dyspepsia remains a problem, continued with gastric protection in the form of a PPI.

Table 1. Medicines that exacerbate dyspeptic symptoms (not exhaustive)

| Non-steroidal anti-inflammatory drugs (NSAIDs) |
| Aspirin (including 75 mg) |
| Corticosteroids |
| Calcium antagonists |
| Antibiotics |
| Bisphosphonates |
| Nitrates (e.g. isosorbide mononitrate) |
| Theophyllines |
| Iron |
| Slow-release potassium |
| Anticholinergic drugs (e.g. tricyclic antidepressants, antipsychotics, oxybutynin) |

3.5 Endoscopy

Endoscopy is the “gold standard” for the investigation of the upper gastrointestinal tract. Its accuracy in detecting organic lesions is higher than 95% and biopsies can diagnose *H. pylori* infection, precancerous conditions, and malignancy; however, diagnostic yield from endoscopy is low once the patient is on acid suppressing drugs.

NICE guidelines recommend immediate (same day) specialist referral for patients presenting with dyspepsia together with significant acute gastro-intestinal bleeding.

NICE guidelines recommend urgent (within two weeks) endoscopy for patients with dyspepsia, also presenting with alarm features (see Table 2).

Routine endoscopy is also recommended, even in the absence of alarm features, for all patients > 55 years old with persistent and unexplained recent onset dyspepsia, i.e. patients whose symptoms have persisted after one to two months, despite *H. pylori* testing and acid suppression therapy. This is because of the increased risk of malignancy in older patients.

Endoscopy referral should also be considered in any patients with previous gastric cancer or surgery, continuing need for an NSAID, raised risk of gastric cancer or anxiety about cancer.

Patients presenting with dyspepsia who are under 55 and without alarm features should be managed empirically.

Table 2. Alarm features in patients with dyspepsia requiring referral for endoscopy

<table>
<thead>
<tr>
<th>Alarm features</th>
<th>Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron deficiency anaemia</td>
<td>Urgent specialist referral for endoscopic investigation (to be seen within two weeks)</td>
</tr>
<tr>
<td>Unexplained weight loss (&gt; 3 kg)</td>
<td></td>
</tr>
<tr>
<td>Epigastric mass</td>
<td></td>
</tr>
<tr>
<td>Evidence of gastrointestinal blood loss (haematemesis/melaena)</td>
<td></td>
</tr>
<tr>
<td>Persistent vomiting</td>
<td></td>
</tr>
<tr>
<td>Suspicious barium meal</td>
<td></td>
</tr>
<tr>
<td>Persistent/progressive dysphagia</td>
<td></td>
</tr>
<tr>
<td>Odynophagia</td>
<td></td>
</tr>
</tbody>
</table>
For patients referred for endoscopy, all antisecretory drugs (PPIs and histamine 2 receptor antagonists) should be stopped two weeks prior to endoscopy as there is a risk of causing healing of early malignant ulcers and promoting overgrowth of normal mucosa in sites of malignant tissue, thus masking early gastric cancer.

3.6 Managing dyspepsia
Dyspepsia has a substantial economic impact and appropriate management is essential to manage healthcare costs.

A flow diagram detailing the management of dyspepsia is provided in Appendix 1.

3.6.1 Clinical history and physical examination
A physical examination along with a careful review of clinical history and medication review should be undertaken for all patients presenting with dyspepsia. The aim is to exclude non-gastrointestinal causes of dyspeptic symptoms such as cardiac or biliary disease and medications. Lifestyle and dietary factors may also be identified. Obesity, smoking, alcohol, coffee, chocolate and fatty foods can exacerbate dyspeptic symptoms.

3.6.2 Lifestyle advice
Lifestyle and dietary factors should be addressed during each presentation with dyspepsia (see Table 3). Individual patients may benefit from simple lifestyle advice, and NICE recommends that advice on healthy eating, weight reduction, caffeine intake and smoking cessation should be offered to all patients presenting with dyspepsia.

Patients should be advised to avoid known precipitants they attribute their dyspepsia to, where possible. It is important to ensure that the efficacy and availability of PPIs does not lead patients to become complacent and choose less healthy lifestyles, as the more general health benefits afforded by the following lifestyle advice should not be lost.

<table>
<thead>
<tr>
<th>Advise people with dyspepsia that symptoms may be improved if they:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lose weight (if the patient is overweight)</td>
</tr>
<tr>
<td>Reduce fatty food intake</td>
</tr>
<tr>
<td>Stop smoking</td>
</tr>
<tr>
<td>Stop or reduce alcohol consumption</td>
</tr>
<tr>
<td>Stop or reduce intake of any food or drink associated with worsening symptoms (e.g. fatty foods, coffee, chocolate)</td>
</tr>
<tr>
<td>Eat meals at regular times, avoiding large or late meals</td>
</tr>
<tr>
<td>Avoid bending over or lying down immediately after eating, and avoid tight belts or clothing</td>
</tr>
<tr>
<td>Use antacid and/or alginate when necessary for immediate symptom relief after meals and at bedtime</td>
</tr>
</tbody>
</table>

Advise people with reflux symptoms when lying down to:

| Avoid meals within 3–4 hours of going to bed                  |
| Raise the height of the head of the bed by a few inches (use of more pillows is ineffective) |
| Use antacid when necessary and/or alginate for immediate symptom relief at bedtime. For patients already receiving a PPI, advise taking the dose in the evening |
3.6.3 Drug treatment
Management of symptoms in primary care is appropriate for most patients rather than routinely seeking a pathological diagnosis\(^1\). NICE advises that self-treatment with antacid and/or alginate continues to be appropriate for many patients; however, additional therapy is appropriate to manage symptoms which persistently affect a patient’s quality of life\(^1\).

Antacids, which neutralise acids in the stomach, can be used for immediate symptom relief\(^1\). They are also sometimes used in functional dyspepsia, although benefit is uncertain\(^1\). Antacids are best given when symptoms occur or are expected, usually between meals and at bedtime.

Alginates taken in combination with an antacid can protect the oesophageal mucosa from acid reflux\(^6\). Alginates can be used for dyspepsia, although benefit is uncertain\(^6\). Alginates are best given when symptoms occur or are expected, usually between meals and at bedtime.

If symptoms persist despite self-management with antacids or alginates, a PPI prescribed at full dose for a one-month course may be considered\(^1\). For more information see section 4.0 Proton Pump Inhibitors.

3.6.4 \textit{H. pylori} testing and eradication
The initial therapeutic strategy for dyspepsia is either empirical treatment with a PPI or testing for and treating \textit{H. pylori}. In patients with predominant heartburn or acid regurgitation, an initial trial of PPI together with lifestyle measures should be tried first. PPIs should be considered first in patients with mainly heartburn and regurgitation\(^5\). For other forms of dyspepsia, there is currently insufficient evidence to guide which should be offered first\(^1\). In adults of any age with dyspeptic symptoms that are persistent or recurrent, the recommended strategy is to test for the presence of \textit{H. pylori} and eradicate if present\(^1\).

\textit{H. pylori} infection is associated with up to 95% of duodenal ulcers and 70% of gastric ulcers, as well as the development of gastric cancer and gastric mucosa-associated lymphoid tissue lymphoma. Infection is often associated with functional dyspepsia, though evidence of its role in this condition is not conclusive. Eradication therapy in \textit{H. pylori}-positive patients will cure most patients with benign peptic ulcers, and prevent ulcer recurrence\(^1\). Only a small proportion of patients with functional dyspepsia will have long-term symptom relief following \textit{H. pylori} eradication\(^5\).

The gold standard non-invasive tests for \textit{H. pylori} are the stool antigen test and \(^13\)C urea breath test. \textit{H. pylori} laboratory serology tests should only be used if locally validated, and office-based serology tests are not recommended as they are not sufficiently accurate\(^1\).

Patients should not have used a PPI for at least 14 days before \textit{H. pylori} testing (note that omeprazole is now available as an over-the-counter [OTC] medicine from pharmacies), and should not have used antibiotics or bismuth for four weeks before the test\(^6\). This is because antibiotics and acid-suppressing drugs can inhibit urease activity within the \textit{H. pylori} bacterium, leading to a false negative near-patient test.

The treatment regimens for eradication of \textit{H. pylori} are detailed in Table 4\(^6\). The two-week quadruple therapy regimen offers the possibility of higher eradication rates compared to one-week regimens, but adverse effects are common and poor compliance is likely to offset any possible gain. They are therefore reserved for therapy following treatment failure and are not recommended in Wales as first-line options.
Table 4. Treatment regimens for the eradication of *H. pylori* infection

<table>
<thead>
<tr>
<th>First line:</th>
<th>First line (penicillin allergy):</th>
</tr>
</thead>
<tbody>
<tr>
<td>One-week triple therapy using:</td>
<td>One-week triple therapy using:</td>
</tr>
<tr>
<td>Lansoprazole 30 mg or omeprazole 20 mg</td>
<td>Lansoprazole 30 mg or omeprazole 20 mg</td>
</tr>
<tr>
<td>Amoxicillin 1 g</td>
<td>Metronidazole 400 mg</td>
</tr>
<tr>
<td>Clarithromycin 500 mg</td>
<td>Clarithromycin 250 mg</td>
</tr>
<tr>
<td>All prescribed twice daily</td>
<td>All prescribed twice daily</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Second line (in cases of treatment failure) – to be documented clearly in medical records:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Two-week quadruple therapy using:</td>
<td>Two-week quadruple therapy using:</td>
</tr>
<tr>
<td>Lansoprazole 30 mg or omeprazole 20 mg twice daily</td>
<td>Lansoprazole 30 mg or omeprazole 20 mg twice daily</td>
</tr>
<tr>
<td>Tripotassium dicitratobismuthate 120 mg four times a day</td>
<td>Tripotassium dicitratobismuthate 120 mg four times a day</td>
</tr>
<tr>
<td>Metronidazole 400 mg three times a day</td>
<td>Metronidazole 400 mg three times a day</td>
</tr>
<tr>
<td>Tetracycline 500 mg four times a day.</td>
<td>Tetracycline 500 mg four times a day.</td>
</tr>
</tbody>
</table>

3.6.5 Community pharmacist support in managing patients with dyspepsia

Community pharmacists are able to offer advice and support to patients with dyspepsia.

Community pharmacist involvement could include:

- lifestyle advice, such as healthy eating, weight reduction or smoking cessation;
- advice on the use of OTC medication for symptom relief;
- referring patients to their GP, for instance where alarm features may be present or medication has not provided adequate symptom relief;
- the provision of primary care services, such as a community-based *H. pylori* test and treat service;
- Medicines Use Reviews – community pharmacists could work with their local practices to focus on patients with dyspepsia and provide consistent recommendations;
- participating in a multidisciplinary audit of dyspepsia prescribing;
- providing patients with a leaflet on PPI (Appendix 4);
- management of the symptoms of dyspepsia through the Common Ailments Service, due to be piloted later in the year.
4.0 PROTON PUMP INHIBITORS

4.1 PPI prescribing
PPIs are licensed and prescribed for a range of indications including:
- short-term treatments of peptic (gastric and duodenal) ulcers;
- eradication of *H. pylori* (in combination with appropriate antibiotics);
- treating dyspepsia and GORD (if medication review and lifestyle advice prove ineffective)
  - for uninvestigated dyspepsia (continuously for 4 weeks or intermittently to control symptoms long-term),
  - for symptomatic functional dyspepsia, after *H. pylori* eradication (for 4 weeks),
  - as an option for mild GORD,
  - for severe GORD (for 4–6 weeks before titrating down to lowest effective dose to maintain remission)
- control of excessive acid secretion in patients with Zollinger–Ellison syndrome;
- prevention and treatment of NSAID-associated ulcers;
- gastro-protection in patients with a history of dyspepsia requiring aspirin following a cardiovascular or cerebrovascular event.

PPIs are used for the short-term treatment of a number of conditions including gastric and duodenal ulcers (4–8 week course), dyspepsia and GORD (normally 4–8 week course) and for eradicating *H. pylori* (1–2 week course). Following completion of the course, the PPI should be reviewed and, if appropriate, discontinued. As recommended by NICE, PPIs should therefore be reviewed 4–8 weeks after initiation. It may be necessary to have repeated short courses of treatments (2–3 times a year) in order to control symptoms, with regular review and cessation of unnecessary therapy. It is also acceptable for patients with dyspepsia to take PPIs on an as-required basis. Additional therapy may be required for patients whose symptoms are problematic and continue to affect quality of life.

Long-term PPI therapy is often prescribed for gastro-oesophageal reflux symptoms associated with a benign oesophageal stricture and/or Barrett’s oesophagus, diagnosed by endoscopy. Other indications for long-term use may include a history of ulcer complication (such as bleeding or perforation) especially in older patients and/or those with major comorbidity or Zollinger–Ellison syndrome.

Gastro-intestinal bleeding and ulceration can occur with NSAID use. The risk of serious gastro-intestinal side-effects varies between individual NSAIDs, with piroxicam, ketoprofen and ketorolac being associated with the highest risk and ibuprofen (up to 1.2 g daily) being associated with the lowest risk. Wherever possible, the NSAID should be discontinued if an ulcer occurs.

In those at high risk of NSAID-induced ulcers, where the NSAID cannot be discontinued, a PPI should be considered for protection against peptic ulceration. Those considered high risk include those aged 65 or older, those with a history of peptic ulcer disease, those taking other medicines which increase the risk of gastro-intestinal side-effects or those with serious co-morbidity (cardiovascular disease, diabetes, renal or hepatic impairment). The PPI should be continued for the duration of the NSAID, but should be reviewed and discontinued when the NSAID is discontinued.

4.2 Safety of long-term PPI use
A clear definition of what is meant by long-term PPI use is lacking and consequently the risks associated with continued therapy are not fully understood. As PPIs have become widely used, evidence has started to emerge regarding their long-term safety and potential for adverse effects, the most significant of which are discussed below.
4.2.1 Rebound hypersecretion
At standard doses, PPIs inhibit 90–98% of acid secretion by binding irreversibly to proton pumps, leading to permanent inactivation. Synthesis of ‘new pumps’ occurs after approximately 24 hours. Acid suppression with PPIs alters normal feedback inhibition, increasing median serum gastrin levels 1.5- to 2-fold, resulting in rebound hypersecretion during treatment discontinuation. Studies looking at the effect of inhibiting acid secretion demonstrated that healthy patients treated with PPIs for eight weeks showed increased gastrin levels, which peaked in the second week after discontinuation of the PPI. The duration of rebound hypersecretion is unknown but some studies show raised gastrin levels three weeks after discontinuation. Other small studies have shown increased hypersecretion for at least eight weeks. This rebound hypersecretion could present as a worsening of symptoms that could be mistaken for disease relapse and may lead to patients being re-initiated on a PPI.

4.2.2 Osteoporotic fractures
Recent research has revealed a link between PPI use and osteoporotic fractures, especially of the hip and vertebrae. This may be due to achlorhydria, resulting in malabsorption of calcium and vitamin B12 with subsequent bone loss. A meta-analysis found that both short-and long-term (> 1 year) PPI use at high and low doses was associated with an increased risk of any fracture (29%), hip fracture (31%) and vertebral fracture (56%). The authors of this study suggest that "clinicians should therefore carefully consider their decision to prescribe PPIs for patients at elevated risk for fracture." It must be noted that the effect of PPIs on bone metabolism and fractures has not been studied in a randomised controlled trial. However, current evidence suggests that for patients prescribed a PPI for one year or more, calcium supplementation could potentially reverse any adverse effects on bone metabolism. The Medicines and Healthcare products Regulatory Agency (MHRA) advice issued in April 2012 stated “There is recent epidemiological evidence of an increased risk of fracture with long-term use of PPIs. Patients at risk of osteoporosis should be treated according to current clinical guidelines to ensure they have an adequate intake of vitamin D and calcium.”

4.2.3 Tubulo-interstitial nephritis
A rare association has been reported between acute tubulo-interstitial nephritis (TIN), an important cause of acute renal failure, and PPIs, occurring between several hours and four months following treatment with a PPI. TIN is difficult to diagnose, with patients typically presenting with non-specific symptoms of acute renal failure, including oliguria, malaise, anorexia, nausea and vomiting. Although TIN might be suggested from clinical and laboratory findings, renal biopsy is the gold standard for diagnosis. The mechanism of drug-induced TIN is unknown, but an immunological mechanism is suspected. Awareness of this rare adverse effect is of high clinical importance as accurate and timely diagnosis could prevent potentially life-threatening renal failure. Initial treatment is immediate discontinuation of the PPI (spontaneous recovery occurs after withdrawal of the offending agent in most cases), in addition to supportive measures which may include corticosteroids. As PPIs are often co-prescribed with NSAIDs, there is a possibility that the PPI could be overlooked as the causative agent in TIN. Any patient presenting with deteriorating renal function, prescribed both a PPI and an NSAID, should have both agents stopped.

4.2.4 Hypomagnesaemia
Both the American Food and Drug Administration and the MHRA have recently warned of the risk of hypomagnesaemia following long-term use of PPIs. This safety information states that hypomagnesaemia occurs most commonly after one year of PPI treatment, and presents with fatigue, tetany, delirium, convulsions, dizziness, and ventricular arrhythmia. Clinicians are advised to consider obtaining serum magnesium levels prior to prescribing PPIs to patients on a long-term basis and to patients also receiving digoxin, diuretics or treatments associated with hypomagnesaemia.
Magnesium supplementation is the normal treatment for hypomagnesaemia but in 25% of cases supplementation alone did not improve low serum magnesium levels and PPI treatment had to be discontinued\(^{19}\).

**4.2.5 Cancer**
Concerns about the possibility of PPIs masking the signs of gastric cancer, either by causing healing of early malignant ulcers or promoting overgrowth of normal mucosa in sites of malignant tissue, are well established and hence the reason for stopping PPIs two weeks prior to endoscopy\(^{21}\). PPI use is associated with increased serum gastrin levels and bacterial overgrowth, resulting in more toxic bile salt formation. Concern has risen that these factors may increase the risk of developing colorectal cancer; however, studies have yet to confirm this\(^{22}\). The authors of one study, which showed no increased colorectal cancer risk, cautioned that such an effect from long-term PPI exposure cannot be ruled out without studying a larger cohort of patients\(^{22}\).

**4.2.6 Clostridium difficile**
The risk of acquiring *C. difficile* associated diarrhoea is approximately 2–3 times higher in PPI users than in non-users and there is a 42% increased risk of recurrent *C. difficile* due to PPI use\(^{23}\). It has therefore been suggested that all PPIs are discontinued in patients diagnosed with *C. difficile*, as they may also increase the risk of recurrence\(^{24}\). Alternatively, it may be appropriate to withhold the PPI for the duration of any future courses of broad spectrum antibiotics.

**4.2.7 Community- and hospital-acquired pneumonia**
Recent initiation of PPI therapy (within the last 30 days) is strongly associated with both community- and hospital-acquired pneumonia (commonly linked with gastric bacterial overgrowth and aspiration)\(^{25,26}\). One trial observed that the risk of hospital-acquired pneumonia was 30% higher in patients taking PPIs\(^{25}\). A separate study found the use of PPIs was associated with an increased risk of community-acquired pneumonia, particularly if started within the previous 14 days\(^{26}\).

The increased risk of *C. difficile* and hospital-acquired pneumonia may be a reason for stopping PPI treatment\(^{2}\).

Clinicians should not be concerned about the risks associated with short-term PPI use when treating acute conditions. However, attention should be paid to conducting regular reviews, prescribing short-term courses of PPIs and ensuring patients learn to manage their condition with alginates and antacids\(^{1}\), ‘stepping up’ to the lowest effective dosage of a PPI to control symptoms when needed\(^{12}\). Long-term PPI exposure may lead to unwanted effects and should be reserved for patients where there is a clinical need. For patients with serious conditions such as gastric or duodenal ulcers, established persistent GORD, NSAID risk or hypersecretory states, the risk of harm during PPI therapy is outweighed by the benefits of treatment\(^{12}\).

**4.3 Choice of PPI**
An analysis of trials of PPIs as treatments for oesophagitis found there is no evidence that one PPI is more effective than any other at equivalent doses, and NICE recommends that the least expensive PPI be used\(^{1}\).

Generic lansoprazole and omeprazole capsules and pantoprazole tablets are considered low acquisition cost (LAC) PPIs and are considered the first-line option when a PPI is indicated. Other formulations of omeprazole and lansoprazole (e.g. dispersible tablets) and branded preparations are less cost effective and lack evidence of improved efficacy or tolerability. Liquid specials are considerably more expensive and should be reserved for hospital specialist initiation. Newer PPIs offer no advantage in terms of clinical efficacy, and less evidence is available in relation to long-term safety\(^{27}\).
If one PPI is ineffective, the patient should be switched to an alternative PPI in preference to increasing the dose above the therapeutic range, as some patients have an increased response to alternative agents.

The costs of selected PPIs in different product forms are given in Table 5.

### Table 5. Cost of selected PPI and alginate preparations

<table>
<thead>
<tr>
<th>Strength</th>
<th>Form</th>
<th>Price £ (for 28)</th>
<th>Strength</th>
<th>Form</th>
<th>Price £ (for 28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mg</td>
<td>Sachet</td>
<td>25.19</td>
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<td>Capsule</td>
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*Note: prescribing 2 x 20 mg capsules is more cost effective than 1 x 40 mg

In 2011, AWMSG endorsed the All Wales Audit/Review Pack – “Reducing the Use of High Acquisition Cost Proton Pump Inhibitors 2011–2013” encouraging the cost-effective use of PPIs. The audit/review pack is available on the AWMSG website if required.

The MHRA has advised that the combination of clopidogrel (indicated for the prevention of atherothrombotic events in patients who have had a myocardial infarction or ischaemic stroke, or who have established peripheral arterial disease) with omeprazole or esomeprazole should be avoided, unless considered essential. Current evidence does not extend this advice to other PPIs. For details of other interactions involving PPIs, please refer to the British National Formulary.

#### 4.4 PPI review

In view of the levels of uncertainty surrounding adverse events from long-term PPI use, prescribers are encouraged to use PPIs judiciously. Treatment should be at the lowest effective dose that controls symptoms, for the minimum period of time. The use of short courses as required and returning patients to self-care with antacid and/or alginate therapy should be encouraged. However, withdrawal of PPIs from patients who do not
need them should not adversely affect quality of life or increase symptom severity or frequency\textsuperscript{31}.

A suggested methodology for a PPI review is shown schematically in Appendix 2. NICE recommends that patients prescribed long-term PPIs are reviewed annually, as there is a potential risk of psychological dependence\textsuperscript{1}. During review, patients should be encouraged to try stepping down or stopping treatment, offered lifestyle advice and advised to avoid precipitants that contribute to dyspepsia. A PPI review toolkit is available within this pack (see Appendix 3).

Rebound hypersecretion, a rise in acid secretion following discontinuation of PPI treatment, may occur following discontinuation of PPI treatment (even for courses as short as eight weeks), leading to an increase of dyspepsia symptoms, and this may be mistaken for disease relapse. To ensure that this does not occur, it is recommended that the dose of PPI is reduced gradually and that an alginate is prescribed for at least two weeks\textsuperscript{2}.

Self-care should be encouraged in all patients with dyspepsia symptoms. Self-care advice includes: lifestyle advice, self-treatment with an antacid or an alginate (prescribed or bought OTC) for immediate relief of symptoms and if necessary low-dose PPI taken “as required”.

4.5 General prescribing points
The following points can help to ensure appropriate prescribing of a PPI:
- Before a PPI is prescribed, clinicians should consider lifestyle changes and review other medications for possible causes of dyspepsia.
- PPIs should only be started or continued where there is a valid documented indication.
- Intermittent courses should be used to control symptoms and/or promote healing, typically up to 4–8 weeks.
- For best results, PPIs should be taken 30–60 minutes before breakfast.
- All newly initiated PPIs should be reviewed after four weeks and repeat PPI prescriptions should be reviewed at a minimum of yearly intervals.
- Long-term care should emphasise patient empowerment by encouraging lifestyle changes and by promoting symptomatic use of alginites/antacids and use of the lowest effective dose of a PPI, ideally in short courses.
- During withdrawal of a PPI, regular alginate therapy should be prescribed for a minimum of two weeks to prevent rebound acid hypersecretion.
REFERENCES


APPENDIX 1: MANAGEMENT OF DYSPEPSIA

(Adapted from All Wales guidance produced by Dr Miles Allison while working with National Leadership and Innovation Agency for Healthcare, 2008, and NICE CG17)

Symptoms of presentation
Indigestion: heartburn, dyspepsia, epigastric/retrosternal pain

Review and consider:
Heart, liver, gallbladder, pancreas, bowel
Excess alcohol
Stopping NSAIDs including aspirin

Offer:
Lifestyle advice

Yes

Alarm features? (see Table 2)

No

Symptom of predominant heartburn?

Yes

Patient aged > 55 years with unexplained and persistent recent onset dyspepsia

Other risk factors for cancer

Manage as for GORD (see NICE1)

No

Manage as uncomplicated dyspepsia (see NICE1)

Persistent or recurrent symptoms

H. pylori faecal antigen test

Positive

Eradicate H. pylori (See Table 4)

Unresolved

Resolved

H. pylori urea breath test

Positive

2nd line eradication (Table 4)

Unresolved

Aged 55+

Aged < 55

Manage as functional dyspepsia (see NICE1)

Consider hospital referral

No

Refer for urgent specialist review/endoscopy (within two weeks)

Refer for routine endoscopy (ideally within six weeks)

Endoscopy findings

Manage as functional dyspepsia (see NICE1)

Manage as peptic ulcer disease (see NICE1)

Manage as GORD (see NICE1)
APPENDIX 2: PPI REVIEW: MAIN ACTION POINTS

Is the patient receiving a PPI on a regular repeat prescription?

Yes

Is there a clinical reason for long-term treatment?

Yes

- Maintain treatment with current PPI and agree period for review
- Ensure the indication is documented in medical notes
- Provide lifestyle advice
- Monitor magnesium
- Ensure adequate intake of calcium and vitamin D in patients at risk of fractures
- Consider future step down where appropriate

No

- Review prescription and address lifestyle issues
- Can PPI be stopped or stepped down?
  - Step down: Consider as required PPI usage with regular self-care*
  - Stop PPI: Initiate gradual dose reduction, with co-prescription of alginate for at least two weeks to reduce rebound hypersecretion
- Manage repeats: Remove from repeat prescribing and prescribe for specific durations
- Record review in notes and monitor progress

No

Symptom return

- Use regular alginate
- Revert to lowest effective PPI dosage as required for up to four weeks
- Consider regular PPI use until symptoms resolve and then re-initiate step down with self-care*

* Self-care
- Patients should receive lifestyle advice and be advised to use alginates first line to control symptoms
- Drugs known to cause gastrointestinal adverse effects should be reviewed
APPENDIX 3: PPI REVIEW TOOLKIT

Purpose of document
The following audit/review has been developed by the Welsh Analytical Prescribing Support Unit (WAPSU). This document is for use by primary care general practitioners to highlight prescribing and cost-effectiveness issues with PPIs. It will be available via the All Wales Medicines Strategy Group (AWMSG) website.

Background
Quality improvement toolkits have been developed to assist general practices in collating and auditing information. These are produced with reference to evidence-based practice and Welsh priorities. They should be seen as good practice and are intended to improve data quality and aid development within the practice.

Improvements in practice will be optimised by multidisciplinary involvement in the audit and team discussion of the results. It is recommended that action plans implemented following this audit are reviewed within six months and re-audit undertaken if possible in 6–12 months.

Aims
- To ensure adequate, timely review of all patients receiving a PPI, in line with NICE guidance
- To ensure all repeat PPI prescribing is appropriate
- To minimise the use of HAC PPIs
- To ensure all patients on long-term PPIs have their magnesium monitored and have an adequate intake of calcium and vitamin D

Objectives
- To identify all patients over the age of 18 years receiving a repeat prescription for a PPI and, where appropriate, discontinue treatment, reduce the dose or move to “as required” administration
- To identify all patients over the age of 18 years prescribed HAC PPIs and where appropriate switch to a LAC alternative

Inclusion criteria
- All patients over the age of 18 years receiving
  - an acute or repeat prescription of a HAC PPI
  - four or more prescriptions (acute or repeat prescription) for a PPI in the last six months

Exclusion criteria
- All patients should be reviewed; however, it may not be appropriate to consider changes to PPI treatment in certain individuals. Consideration should be given to whether a previous PPI switch has been attempted, and to other medical situations e.g. chemotherapy, palliative care or a mental health condition, where changes to medication would be inappropriate
- Under 18 years
- Patients in whom there is a continued need for an NSAID, or with a history of benign oesophageal stricture, Zollinger–Ellison or Barrett’s oesophagus, are not appropriate for “as required” treatment or self-care

Preparation
- The appropriate clinician should brief practice staff about the review
- Local community pharmacists should be informed of the review to enable them to provide supporting advice
The Review Process

1.0 Identify patients receiving a prescription for a PPI who meet the inclusion criteria

Use the GP clinical database system to perform a search for all patients over the age of 18 years who:

- Have been prescribed a HAC PPI in the last six months (acute or repeat prescription) – review according to All Wales Audit/Review Pack – “Reducing the use of high acquisition cost proton pump inhibitors 2011–2013”\[29\], if not previously reviewed.
- Have a PPI on their repeat prescription (for 28 days or equivalent)
- Have collected four or more prescriptions for a PPI in the last six months.

Include the generic name and brand name for each drug in the search. Some computer systems will allow a search on the action group for PPIs to avoid having to enter the drugs individually.

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Brand name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esomeprazole</td>
<td>Nexium®</td>
</tr>
<tr>
<td>Pantoprazole</td>
<td>Protium®</td>
</tr>
<tr>
<td>Rabeprazole</td>
<td>Pariet®</td>
</tr>
<tr>
<td>Omeprazole</td>
<td>Losec®</td>
</tr>
<tr>
<td>Lansoprazole</td>
<td>Zoton®</td>
</tr>
</tbody>
</table>

Note: remember to include all formulations of PPIs including dispersible tablets and liquid specials.

2.0 Complete the data collection sheet

A sample data collection form for PPI review has been included (see Appendix 5). This can be adapted for local use. Use the patients’ medical records to complete these forms.

3.0 Identification of patients suitable for review/discontinuation of treatment

Review patients for their continuing need for a PPI, or their suitability for a reduction in dose, “as required” use or a switch to a cost-effective alternative (e.g. change from a HAC to a LAC PPI, change to a more cost-effective formulation). Use the flow diagram in the dyspepsia and PPI guideline (see Appendix 2).

4.0 Authorise the change

If the review is completed by a non-GP, make sure that each dose reduction, move to “as required” management or discontinuation of use is authorised by the patient’s own GP or as agreed within the practice.

All reviews and dose changes should be clearly documented within the medical notes. If the change is not authorised, the reason for this should be documented in the patient’s medical notes.

If a patient is to remain on a HAC PPI, document the reason for this in the patient’s medical records.

In all cases where the review results in a patient remaining on long-term regular PPIs, document the reason for this in the patient’s medical records. All patients remaining on long-term regular PPIs should be counselled on adequate calcium and vitamin D intake, and should have a blood test to monitor serum magnesium levels periodically during treatment, especially those who will take a PPI concomitantly with digoxin or drugs that may cause hypomagnesaemia (e.g. diuretics).
5.0 Changes to the patient’s medical record
Remove the PPI from repeat prescription in all patients who have not collected a prescription for the last six months. This will prompt a review of symptoms if a request for the PPI is made again.

Add the details of the new medication and changes in dose or directions to the patient’s current medication record, ensuring that the non-proprietary (generic) formulation is selected.

Remove the medication to be discontinued from the patient’s repeat prescribing list on the current medication record.

Document the reason for the change in the patient’s clinical record e.g. therapeutic substitution, switch to LAC PPI or removal of high risk medication such as an NSAID. Ensure indication for PPI is documented.

6.0 Inform the patient about changes to their medication
Send the appropriate letter to all patients, informing them of the changes made to their medication.

Alternatively, a letter inviting a patient to attend for review and discussion could be used and changes made during a face to face consultation.

A Patient Information Leaflet (PIL), “Proton Pump Inhibitors (PPIs) for the Treatment of Indigestion” (in English and Welsh), is provided in Appendix 4 and is also available on the AWMSG website.

7.0 Keep a record
Keep a separate record of all patients where the PPI dose has been altered or stopped.

8.0 Arrange follow-up monitoring
Arrange a follow-up of selected patients, where considered necessary.

9.0 At follow-up
Ensure that the symptoms remain controlled, and if not discuss an appropriate way forward to regain control.

Record those patients where the switch is unsuccessful and any reasons why, in order to avoid future attempts.

10.0 Summary of review
Use the summary form provided (see Appendix 6) to review all changes made and measure the effectiveness of the change programme.
APPENDIX 4: PPI PATIENT INFORMATION LEAFLET (ENGLISH AND WELSH)

Patient Information – Proton Pump Inhibitors for the Treatment of Indigestion

INDIGESTION
Indigestion (dyspepsia) is usually pain or discomfort in the upper abdomen or a burning pain felt behind the breastbone. This burning pain is commonly called heartburn.

PROTON PUMP INHIBITORS (PPIs)
A PPI (e.g. omeprazole, lansoprazole, esomeprazole, pantoprazole, rabeprazole sodium) is a medicine that reduces the amount of acid that your stomach makes. By lowering the acid level, it can help to relieve the symptoms of indigestion.

A PPI may be prescribed by your doctor or bought with advice from a pharmacist.

How can I improve my indigestion symptoms?
- Keep to a healthy weight.
- Avoid food and drink that make your symptoms worse (e.g. spicy or fatty foods, chocolate, coffee, cola drinks, orange juice).
- Eat meals at regular times.
- Avoid large or late meals and avoid bending over or lying flat immediately after eating.
- Avoid medicines that can make symptoms worse, e.g. some painkillers. Ask your doctor or pharmacist which medicines are safe to take.
- If your symptoms are worse at night, try raising the head of the bed by 10–15 cm (4–6 inches) using blocks under the legs of the bed.
- Stop or reduce your alcohol consumption. Do not regularly drink more than 14 units per week. If you do drink as much as this, it is best to spread this evenly across 3 days or more. If you feel that you have a problem with alcohol, talk to a healthcare professional.
- Stop smoking. Discuss ways to quit smoking with your doctor or pharmacist or call “Stop Smoking Wales” free on 0800 085 2219.

Should I take a PPI?
Your doctor will discuss with you whether a PPI might be helpful and how long you should take it for. This will depend on why you are taking it, as PPIs can be used for lots of different conditions.

How long should I take my PPI for?
To start with, you may be given a PPI for 4 weeks. If your symptoms continue then you may be prescribed another 4-week course of treatment.

Many people find that after 4–8 weeks of taking a PPI their symptoms are better; the PPI should then be stopped as you no longer need it.

Why should I stop my PPI?
Taking PPIs for a long time can have unwanted effects, so you should only take PPIs long term where there is a definite need.

Unwanted effects of long-term PPIs could include:
- thinning of the bones (osteoporosis),
- masking of the signs of stomach cancer,
- increased risk of infections (e.g. Clostridium difficile and pneumonia).

However, some people with certain conditions, e.g. severe oesophagitis, strictures, Barrett’s oesophagus or Zollinger–Ellison syndrome, need long-term PPI treatment. People taking medicines that can cause peptic ulcers may also need long-term PPI treatment. Your doctor will be able to tell you if you need to take a PPI long term.

How will I stop my PPI?
Some people find that when they stop taking their PPI their symptoms seem worse, especially if they have been taking it for a long time. This is because if you take a PPI for more than a few weeks, your stomach will increase its ability to make acid. This means that for a while after you stop taking your PPI, the acid levels in your stomach may be higher than before you started your treatment. To help with this, you may have your treatment ‘stepped down’ to one of the following options:

1. Stop PPI. You may be advised to stop taking your PPI and use an antacid and/or alginate if you still have symptoms. An antacid neutralises the acid in your stomach, and an alginate prevents acid flowing into your oesophagus (food pipe). If these fail to help, you should return to see your doctor.
2. Take PPI only when needed. You may be advised to take your PPI only when you have symptoms. When the symptoms are relieved (often after a few days) you stop taking the PPI.
3. Reduce PPI dose. If you have taken your PPI for a number of months, particularly if you have been taking a high dose, your doctor may reduce your PPI dose for a few weeks before stopping completely.

What if my symptoms come back?
Your doctor may also prescribe you an antacid and/or alginate. These can help to control your symptoms, if needed, until your acid levels return to normal. Alternatively, your doctor may prescribe a medicine known as an H₂-receptor antagonist, e.g. ranitidine, which works in a similar way to a PPI but with fewer long-term side effects.

If you have symptoms when you stop your PPI, and you have not been offered any other medicine, or you think the medicine you have been given is not working, you should speak to your doctor or pharmacist.

It is common for symptoms to come back again, sometimes after a number of months. If this happens, you should speak to your doctor or pharmacist.

What should I do if I develop problems at any time?
You should see your doctor if your symptoms do not get any better, if they get worse or if you have:
- Vomiting, especially if this contains blood or material that looks like coffee grounds;
- Dark, sticky bowel movements;
- Difficult or painful swallowing;
- Unexplained weight loss;
- Chest pain that gets worse with or after exercise, or that goes into your chin or left shoulder. These may be signs of a heart problem.
Gwybodaeth i Gleifion – Atalwyr Pwmp Proton ar gyfer Trin Diffyg Traul

DIFFYG TRAUL
Poen neu anghyssurwaith yn yr abdonen uchaf, neu boen ll osgoi a deimlir y tu ól i asgrwn y frest, yw diffyg traul (dyspepsia).

ATALWYR PWMP PROTON (PPIs)
Meddyginaeth sy’n lleihau faint o asid, gall helpu i liniaru symptomau diffyg traul (esomeprazole, pantoprazole, sodiwm rabeprazole). Drwy Meddyginiaeth sy’n lleihau faint o asid y mae eich stumog (ATALWYR PWMP PROTON (dyspepsia)).

Poen neu anghyssurwch yn yr abdomen uchaf, neu boen DIFFYG TRAUL

Sut allaf i wella fy symptomau diffyg traul?

1. Stopio PPI. Efaffai y cynghorhir chi i stopio cyrmwd eich PPI a defnyddio gwirthasid a/neu alginad os byddwch yn dal i gael meddyg. Mae gwirthasid yn niwratrieddio’r asid y mae eich stumog, ac mae alginad yn atal asid rhag llifo i’ch oesosfagws (pibell fwyd). Os na fydd y rhain yn helpu, dylech fynd yn ôl i weld eich meddyg.

2. Cymryd PPI dim ond pan fo angen. Efaffai y cynghorhir chi i gynghor gyda’r meddyg eich PPI dim ond pan fo anghyssurwch ymddangos ym dynod o fstoio'r stumog. Ef allaif y cynghorhir chi i stopio cyrmwd eu PPI am dymor hir, a chaiff PPI i niwtraleiddio'r asid y mae eich stumog am ychydig wythnosau, cyn ei stopio’n llwyr.

Beth os bydd fy symptomau’n dychwelyd?

Gall eich meddyg helfred yw’r oedolyn a/neu alginad a/neu Meddyginaeth sy’n lleihau faint o asid. Fodd bynnag, mae pobl sydd â rhai cyflyrau, megis llid yr corff, neu sy’n mynd i mewn i’ch gên neu’ch ysgwydd, angen triniaeth pob dydd neu ddyddu neu hunain.-

Beth ddylwn ei wreudd os caf broblemau ar un rhwng?

Dylech yna llyncu neu boen wrth lyncu; Carthion tywyll a gludiog; Chwydu, yn arbennig os yw’n cynnwys gwaed neu dauodd. Os cewch anys bosib chwith. Gall y rhain fod yn arwyddion o broblem y galon. Os cewch unrhyw un o’r canlynol:

- Ceisiwch ddefnyddio niwtraleiddio'r asid y mae eich stumog.
- Ceisiwch dyfrio'r asid y mae eich stumog am ychydig wythnosau, cyn ei stopio’n llwyr.
- Os na fydd y rhain rhag llifo i’ch oesoffagws (pibell fwyd), gall y rhain helpu i liniaru symptomau diffyg traul (dyspepsia).

Os dweudch yna llyncu neu boen wrth lyncu, carthion tywyll a gludiog, chwydu, neu gwaed neu dauodd, gall y rhain fod yn arwyddion o broblem y galon. Os dweudch nich hyn, gall y rhain helpu i niwtraleiddio'r asid y mae eich stumog.

A ddylwn i gymryd PPI?

Bydd eich meddyg yn trafod gyda chi a fyddai PPI yn ddefyndydiol ac am faint y dylech ei gymryd. Bydd hyn yn dibynnau ar pam eich bod ei angen, gan y gellir cyrmwd PPI ar gyfer nifer o wahanol gyflymru.

Am faint ddyln i gymryd fy PPI?

I ddechrau, efaffai y rhoddir PPI a chi am 4 wythnos. Os bydd eich symptomau’na parhau yna efaffai y rhaglordir ef i chi am gwsr triaithia 4 wythnos arall.

Bydd llawer o bobl yn gweld bod eu symptomau’u well wedi 4–8 wythnos o gymryd PPI; yna dyled stopio ei gymryd gan nad ydych ei angen mwyach.

Pam ddylyn i stopio PPI?

Gall cyrmwd PPI am amser hir gael eiffelliaith nas dymunir, felly dylech byd ei ddefnyddio niwtraleiddio'r asid y mae eich stumog.

Galliai eiffelliaith nas dymunir PPI tymor hir yn hynny:

- teneuor’r esgryn (osteoporosis),
- cuddio arwyddion cysyn ystymog, e.e. Clostridiwm difficile a niwtraleiddio,
- cynydd yn y perygl o gael ragnodi gan eich meddyg ne’i angen mwyach.

Fodd bynnag, mae pobl sydd â thalwgyn llawer o gymryd PPI ac am faint o gymeriad ym dref ychydig os byddwch ynddynt, a dwinwch i wedi ei stopio ei PPI am dymor hir. Efaffai hefyd y bydd pobl sy’n cyrmwd meddyginiaethau a all achosi briwiau peptig angen cymryd PPI am dymor hir. Bydd eich meddyg yn gallu dweud wrthych a oes gwychny gyflywyr sy’n golygu bod angen i chi i gymryd PPI am dymor hir.

Gall y rhain helpu i niwtraleiddio'r asid y mae eich stumog am ychydig wythnosau, cyn ei stopio’n llwyr.

1. Stopio PPI. Efaffai y cynghorhir chi i stopio cyrmwd eich PPI a defnyddio gwirthasid a/neu alginad os byddwch yn dal i gael meddyg. Mae gwirthasid yn niwtraleiddio’r asid y mae eich stumog, ac mae alginad yn atal asid rhag llifo i’ch oesosfagws (pibell fwyd). Os na fydd y rhain yn helpu, dylech fynd yn ôl i weld eich meddyg.

2. Cymryd PPI dim ond pan fo angen. Efaffai y cynghorhir chi i gynghor gyda’r meddyg eich PPI dim ond pan fo anghyssurwch ymddangos ym dynod o fstoio'r stumog. Ef allaif y cynghorhir chi i stopio cyrmwd eu PPI am dymor hir, a chaiff PPI i niwtraleiddio'r asid y mae eich stumog am ychydig wythnosau, cyn ei stopio’n llwyr.

Beth os bydd fy symptomau’n dychwelyd?

Gall eich meddyg helfred yw’r oedolyn a/neu alginad a/neu Meddyginaeth sy’n lleihau faint o asid. Fodd bynnag, mae pobl sydd â rhai cyflyrau, megis llid yr corff, neu sy’n mynd i mewn i’ch gên neu’ch ysgwydd, angen triniaeth pob dydd neu ddyddu neu hunain.-

Beth ddylwn ei wreudd os caf broblemau ar un rhwng?

Dylech yna llyncu neu boen wrth lyncu; Carthion tywyll a gludiog; Chwydu, yn arbennig os yw’n cynnwys gwaed neu dauodd. Os dweudch nich hyn, gall y rhain helpu i niwtraleiddio'r asid y mae eich stumog.

1. Stopio PPI. Efaffai y cynghorhir chi i stopio cyrmwd eich PPI a defnyddio gwirthasid a/neu alginad os byddwch yn dal i gael meddyg. Mae gwirthasid yn niwtraleiddio’r asid y mae eich stumog, ac mae alginad yn atal asid rhag llifo i’ch oesosfagws (pibell fwyd). Os na fydd y rhain yn helpu, dylech fynd yn ôl i weld eich meddyg.

2. Cymryd PPI dim ond pan fo angen. Efaffai y cynghorhir chi i gynghor gyda’r meddyg eich PPI dim ond pan fo anghyssurwch ymddangos ym dynod o fstoio'r stumog. Ef allaif y cynghorhir chi i stopio cyrmwd eu PPI am dymor hir, a chaiff PPI i niwtraleiddio'r asid y mae eich stumog am ychydig wythnosau, cyn ei stopio’n llwyr.

3. Lleihau dos PPI. Os ydych wedi bod yn cymryd eich PPI am nifer o fisoedd, yn enwedig os ydych wedi bod yn cymryd dyspepsia,可能会对胃有影响。这样可能会导致胃酸分泌过多，从而引起胃痛和其他不适症状。因此，如果您发现自己有胃痛或其他不适症状，应立即停止使用相间的PPI，并咨询医生或药剂师。医生或药剂师可能会建议您采取一些措施来减轻症状，例如改变饮食习惯或使用其他药物。在任何情况下，如果您怀疑自己患有胃痛或其他不适症状，应立即寻求医疗帮助。
## APPENDIX 5: INDIVIDUAL DATA COLLECTION FORM FOR PPI REVIEW

<table>
<thead>
<tr>
<th>Patient name/ID</th>
<th>Drug</th>
<th>Dose</th>
<th>Formulation</th>
<th>Last collected</th>
<th>What is the dosing schedule?</th>
<th>Regularly</th>
<th>PRN</th>
<th>Unknown</th>
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</thead>
</table>

**Who initiated/recommended current PPI? (Tick most appropriate)**

<table>
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<th>Option</th>
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<tbody>
<tr>
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<td></td>
</tr>
<tr>
<td>Pharmacist</td>
<td></td>
</tr>
<tr>
<td>Hospital specialist</td>
<td></td>
</tr>
<tr>
<td>Other, please specify</td>
<td></td>
</tr>
</tbody>
</table>

**Is the patient on any medication which may interact with the PPIs (most importantly clopidogrel, warfarin, phenytoin – care with omeprazole/esomeprazole)?** Please state

**Indication for PPI? (Tick all that apply)**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Ticks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endoscopically confirmed GORD</td>
<td>Uninvestigated dyspepsia</td>
</tr>
<tr>
<td>Endoscopically confirmed peptic ulcer disease</td>
<td>Uninvestigated reflux disease</td>
</tr>
<tr>
<td>Endoscopically negative reflux disease or non-ulcer dyspepsia</td>
<td>Benign oesophageal stricture</td>
</tr>
<tr>
<td>Zollinger–Ellison syndrome</td>
<td>Barrett’s oesophagus</td>
</tr>
<tr>
<td>Uncertain diagnosis, please specify</td>
<td>Other, please specify</td>
</tr>
</tbody>
</table>

**Prophylaxis of drug-induced dyspepsia/ulceration, please specify drug(s)**

**Is there opportunity to review the drug(s)?**

**H. pylori testing (if indicated)**

<table>
<thead>
<tr>
<th>Has the patient been tested for <em>H. pylori?</em></th>
<th>Yes</th>
<th>No</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>If positive, has this patient had <em>H. pylori</em> eradication therapy?</td>
<td>Yes</td>
<td>No</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

**Has the patient received lifestyle advice?**

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
</table>

**Has a previous switch/review been undertaken? If yes, give details**

**Has the patient been on another PPI previously? If yes, give details**

**Has the dosage of the PPI been changed during the current course of treatment? If yes, give details**

**Is the patient on long-term PPIs (> 1 year)?**

**If yes:**

<table>
<thead>
<tr>
<th>Has the patient had a PPI review in the last 12 months?</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Has the patient had their serum magnesium monitored? (No clear guidance on frequency of monitoring; important in patients on long-term PPIs who are also receiving digoxin, diuretics or other drug treatments known to cause hypomagnesaemia)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Has the patient been advised about calcium and vitamin D intake/taking calcium and vitamin D supplements? (Patients at risk of osteoporosis should be treated in line with current guidelines to ensure adequate calcium and vitamin D)</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

**Is there a reason for not reviewing PPI in this patient (see possible exclusions)?**

Yes, please specify

**Has the patient been identified as being able to change from their current PPI/dose to a more suitable alternative?**

Yes

No (continue on current PPI)

Unsure (refer to GP for review)

**If yes, what action is the most appropriate for this patient?**

Reduce dose of LAC PPI at regular usage – state dose and directions

Reduce to LAC PPI at PRN usage with self-care – state dose

Switch from HAC PPI to LAC PPI – state PPI and dose

Stop PPI (remove PPI from repeat if not collected for > six months). If long-term PPI, consider reducing PPI dose before stopping or provide acute prescription of
Welsh Analytical Prescribing Support Unit

- an alginate for 2–4 weeks to prevent rebound hypersecretion
- Other, please state

**Proposed action (tick when completed)**
- Send letter to patient inviting them to make appointment for review
- Send letter to patient informing them of change, enclose PIL explaining change

Action to be completed by:

<table>
<thead>
<tr>
<th>Completed by</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reviewed and authorised by (GP sign)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### APPENDIX 6: GP PRACTICE SUMMARY FORM

**GP Practice:**

<table>
<thead>
<tr>
<th>Pre-review</th>
<th>Date of Review</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PRACTICE LIST SIZE</th>
<th>Percentage of practice population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients in the practice identified in step 1</td>
<td></td>
</tr>
<tr>
<td>Number of patients prescribed a LAC PPI*</td>
<td></td>
</tr>
<tr>
<td>Number of patients prescribed a HAC PPI</td>
<td></td>
</tr>
<tr>
<td>Number of patients suitable for inclusion in the review</td>
<td></td>
</tr>
</tbody>
</table>

*LAC PPIs are lansoprazole 15 mg and 30 mg capsules, omeprazole 10 mg and 20 mg capsules and pantoprazole 20 mg and 40 mg tablets only.*

### Documentation

<table>
<thead>
<tr>
<th>Quantity</th>
<th>Percentage of patients reviewed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients with a documented indication for therapy when PPI initially prescribed</td>
<td></td>
</tr>
<tr>
<td>Number of patients with a documented indication for long-term use</td>
<td></td>
</tr>
<tr>
<td>Number of patients who have had lifestyle advice documented in their notes within the last 12 months</td>
<td></td>
</tr>
<tr>
<td>Number of patients who have had a review of their PPI in the last 12 months</td>
<td></td>
</tr>
<tr>
<td>Number of patients on long-term treatment who have had their serum magnesium monitored</td>
<td></td>
</tr>
<tr>
<td>Number of patients with whom calcium and vitamin D intake has been discussed/supplements being taken</td>
<td></td>
</tr>
</tbody>
</table>

### Summary of interventions made

<table>
<thead>
<tr>
<th>Quantity</th>
<th>Percentage of patients reviewed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of patients: Dose of LAC PPI reduced</td>
<td></td>
</tr>
<tr>
<td>Total number of patients: LAC PPI reduced to &quot;as required&quot; use and self-care</td>
<td></td>
</tr>
<tr>
<td>Total number of patients: Stop PPI (encourage self-care with antacid/alginate)</td>
<td></td>
</tr>
<tr>
<td>Total number of patients: Switch from HAC PPI to LAC PPI</td>
<td></td>
</tr>
</tbody>
</table>

### Post review summary

<table>
<thead>
<tr>
<th>Number of patients prescribed a LAC PPI*</th>
<th>Number of patients prescribed a HAC PPI</th>
<th>Percentage of practice population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients in the practice on a PPI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of patients prescribed a LAC PPI*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of patients prescribed a HAC PPI</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>