LEARNING OBJECTIVES:
Upon successful completion of this lesson, pharmacists should be able to:
1. Describe the epidemiology of GERD and its associated risk factors.
2. Describe symptoms of GERD and the level of severity in their patients.
3. Assist patients in making informed decisions about their therapy.
4. Understand the importance of continued follow-up with these patients and recognize when patients will require further investigations.
5. Accurately discuss the potential for drug interactions and identify potential interactions based on the current literature.
6. Describe how current provincial regulations can expand the pharmacist’s ability to provide ongoing care to GERD patients (e.g., through prescription adaptations).

INSTRUCTIONS
1. After carefully reading this lesson, study each question and select the one answer you believe to be correct. Circle the appropriate letter on the attached reply card or answer online for immediate results at www.canadianhealthcarenetwork.ca.
2. To pass this lesson, a grade of at least 70% (18 out of 25) is required. If you pass, please retain a record in your learning portfolio.

ANSWERING OPTIONS
A. Answer online for immediate results at www.canadianhealthcarenetwork.ca.
B. Mail or fax the printed answer card to (416) 764-3937. Your reply card will be marked and you will be advised of your results within six to eight weeks in a letter from Rogers Publishing. NOTE: All faxed or mailed reply cards must be submitted one month before lesson expiry date.

PROVINCIAL CASE STUDY
This CE lesson includes a detailed case study illustrating how pharmacists in B.C. may choose to exercise authorities granted under Professional Practice Policy #58, the “Protocol for Medication Management – Adapting a Prescription,” during the provision of patient care.
patient with typical and atypical GERD. Age and sex do not seem to play a role in the epidemiology of GERD but there is some information to suggest that there may be a genetic predisposition to the development of symptoms.2,6

Certain medications can influence LES pressure (Table 1) and may precipitate GERD. Behavioural or lifestyle choices that may trigger GERD symptoms include smoking, alcohol consumption, weight gain or obesity, eating large meals, caffeine intake, stress, lying down after eating, or consuming food or drinks that are considered acidic.

Existing co-morbid conditions that are typically associated with, or can increase the risk of, GERD include pregnancy, irritable bowel syndrome, anxiety, depression, and peptic ulcer disease.2 Conditions that are aggravated by GERD include chronic cough, chronic laryngitis and asthma.7

### Table 1. Medications that can affect lower esophageal sphincter pressure6,20

| Anticholinergic medications including: atropine, hyoscyamine, oxbutynin |
| β – Adrenergic agonists: salbutamol, salmeterol, terbutaline, fenoterol |
| α – Adrenergic antagonists: prazocin, terazocin |
| Calcium channel blockers: diltiazem, nifedipine, verapamil |
| Narcotics: morphine, codeine, |
| Progesterone |
| Theophylline |
| Tricyclic antidepressants: amitriptyline |
| Caffeine |

### Diagnosis

The typical presentation of a patient with GERD include complaints of “heartburn,” that is, a retrosternal – beneath the breastbone — burning sensation which may or may not rise to the back of the throat and/or regurgitation (acidic stomach contents rising into the throat or mouth). Any chronic or recurrent pain or discomfort centred in the upper abdomen (i.e., the epigastrum) should not be misdiagnosed as GERD and these patients should be referred to their physician for possible diagnosis of dyspepsia. Other symptoms may also occur as the result of GERD (Table 2). These can be divided into two categories: esophageal and extraesophageal.1,7 It is important to recognize that patients with GERD may also have evidence of esophageal injury.

GERD patients can be divided into two groups: those with non-erosive reflux disease (NERD), i.e., no endoscopic evidence of injury (also known as endoscopy-negative reflux disease or ENRD) and those with reflux esophagitis.

### Table 2. Esophageal vs. extraesophageal symptoms of GERD1

<table>
<thead>
<tr>
<th>Esophageal symptoms</th>
<th>Extraesophageal symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heartburn</td>
<td>Cough</td>
</tr>
<tr>
<td>Regurgitation</td>
<td>Sore throat</td>
</tr>
<tr>
<td>Non-cardiac chest pain</td>
<td>Hoarseness</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>Shortness of breath</td>
</tr>
<tr>
<td>Nausea</td>
<td>Wheezing</td>
</tr>
</tbody>
</table>

### Table 3. Alarm features: when to refer to a physician1

| Chest pain |
| Dysphagia (particularly progressive solid food dysphagia) |
| Vomiting |
| Evidence of gastrointestinal blood loss (hematemesis, melena, iron deficiency anemia) |
| Jaundice |
| Involuntary weight loss |
| Odynophagia (painful swallowing) |
| Choking (cough, dyspnea, hoarseness) |

Pharmacists can diagnose GERD based on the presence of heartburn and/or regurgitation and on whether the patient considers the symptoms to be troublesome.1,7 It is important to have patients describe their symptoms completely and not simply accept the term “heartburn” when people are seeking advice on medication selection. This will ensure that patients meet the criteria for GERD and that they are not experiencing dyspepsia or other symptoms that may require further investigations and physician referral.

Unless alarm features (Table 3) are present, the initial diagnosis of GERD can be made without referral to a physician in patients with typical reflux symptoms.

The presence of alarm features should prompt pharmacists to refer patients to their physicians or to a hospital emergency room immediately for further investigations to rule out other conditions or complications of GERD (Table 4).

Alarm features include vomiting, evidence of gastrointestinal tract blood loss, anemia, involuntary weight loss, dysphagia (difficulty swallowing), or chest pain.1

Although dysphagia is considered an alarm feature, if it is mild and resolves with acid suppression therapy, it can be diagnostic for GERD. On the contrary, if the patient is experiencing solid food dysphagia that is worsening and not responsive to two to four weeks of acid suppression therapy, further investigations should be undertaken immediately to eliminate the possibility of other more serious conditions, including malignancy and esophageal stricture.1

If chest pain is the primary complaint, patients should be referred to their physicians for further investigations to rule out cardiac disease before any other diagnosis can be assigned. Chest pain caused by GERD can be indistinguishable from ischemic cardiac pain, even without the typical symptoms of heartburn or regurgitation.1

Although the diagnosis of GERD can be arrived at independently of the frequency and severity of symptoms, these factors are important in developing the right management course for the patient. Patients who experience low intensity symptoms twice...
a week or less, and the symptoms do not significantly influence their daily lives, are considered to have mild disease. Patients who experience more prolonged discomfort that occurs at least three times per week, and which affects their daily lives, are considered to have moderate or severe disease.¹

Long-term therapy for reflux will be, in all likelihood, necessary in patients with esophageal injury diagnosed by endoscopy. This group includes patients with Barrett’s esophagus, which is defined as metaplastic changes of the esophageal lining likely caused by chronic esophagitis due to reflux. This finding puts the patient at an increased risk of malignancy. Other indications for long-term antireflux therapy are erosive esophagitis, ulceration, hemorrhage, or esophageal strictures.²,³

Endoscopy is not required to make the diagnosis of GERD; however, in the presence of alarm features this is the preferred and most proven diagnostic test for viewing the esophagus and upper gastrointestinal tract. Endoscopy is indicated in the presence of alarm features or atypical symptoms or to diagnose Barrett’s esophagus in patients who have been experiencing GERD symptoms for 10 years or more.¹

Ambulatory pH monitoring may be used when patients are demonstrating atypical symptoms or continued symptoms despite antisecretory medication. Barium swallow tests are not considered to be useful in the diagnosis of GERD due to the lack of sensitivity and specificity.¹

**Management**

Once a patient has met the criteria and definition for GERD, management depends on the severity of the symptoms. When patients consult their pharmacists about their symptoms it is an opportune time to question them about any concurrent medical conditions, medications or other triggers that may be causing their symptoms. Most patients with GERD will self-diagnose and self-treat prior to talking to their pharmacist, so it is important to ask them about what they have tried previously.

**Patients with mild, infrequent symptoms**

For mild disease, where symptoms occur no more than twice weekly, the typical route for treatment begins with advising patients on lifestyle modifications (Table 5) or avoidance of triggers. These can include losing weight, decreasing alcohol intake, avoiding foods that trigger reflux, not lying down after meals, elevating the head of the bed, stopping smoking, avoiding acidic drinks and not wearing tight clothing.¹ In the majority of cases, even those with mild symptoms, lifestyle modifications alone will not be sufficient to eliminate GERD.

In the treatment of patients with mild GERD, studies have shown that OTC products such as antacids, alginites and H2RAs are safe and effective first line treatments.¹

Patients with mild or infrequent GERD should be questioned about the predictability of their symptoms. If, for instance, their symptoms occur after eating a large meal, suggesting treatment with H2RAs, such as ranitidine or famotidine, 30–60 minutes prior to a meal would be a valid first step. Patients who consider their symptoms to be unpredictable would more likely benefit from alginites or antacids taken as needed when symptoms occur. (Figure 1) Helping patients choose from the vast selection of OTC products available for the treatment of reflux can provide a great opportunity to open the doors for discussion and follow up should the medication be unsuccessful in treating their symptoms. (Table 7)

**Patients with moderate/severe, frequent symptoms**

Patients who describe moderate or severe GERD, that is, symptoms that occur more than three times per week and which affect their quality of life, should be referred to their physicians for treatment.

Treatment of moderate to severe GERD requires acid suppression therapy. It has been shown that the severity of esophageal injury and symptoms are related to the amount of time that the gastric pH is less than 4.0.¹ The two groups of drugs that can achieve this are H2RAs and PPIs.

H2RAs block histamine receptors on parietal cells, inhibiting gastric secretion and therefore decreasing the acidity of gastric contents. PPIs cause irreversible proton pump inhibition in the parietal cell, decreasing gastric acid secretion.

PPIs have been shown to be superior to H2RAs in several different outcomes in two meta-analyses. The first meta-analysis showed that PPIs heal esophagitis almost twice as quickly as H2RAs.⁸ A second meta-analysis demonstrated an almost twofold superiority in effectiveness of PPIs over H2RAs.¹⁰ The inferiority of H2RAs may be due to several different mechanisms. First, the effect of H2-receptor antagonism on the parietal cell lasts only for a short period, so twice daily dosing is needed. Secondly, the effects of H2RAs are negatively affected by food. Thirdly, tolerance develops to H2RAs and increasing the dose has not been shown to overcome this effect.¹

PPIs are much more effective in keeping the pH of gastric acid above four for prolonged periods of time and they can therefore provide more healing and symptom relief in patients with GERD when compared with H2RAs. Among the PPIs, equivalent doses have been arrived at by assessing their relative potencies through analyses of pharmacokinetic, pharmacodynamic and clinical data.³,¹¹ (Table 7)

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**Table 5. Lifestyle interventions**¹²

<table>
<thead>
<tr>
<th>Foods to avoid</th>
<th>Lifestyle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acidic foods: citrus fruit; tomatoes; onions; carbonated beverages; spicy foods</td>
<td>If patients have symptoms after eating: smaller meals; avoid lying down after meals</td>
</tr>
<tr>
<td>Foods that can cause gastric reflux: fatty or fried foods; coffee, tea and caffeinated beverages; chocolate; mint</td>
<td>If patients have night time symptoms: Do not lie down after eating; similarly avoid eating within 3 hours of bedtime; raise the head of the bed</td>
</tr>
<tr>
<td>Foods that trigger symptoms for a specific patient</td>
<td>Abdominal obesity: don’t wear tight clothing</td>
</tr>
<tr>
<td></td>
<td>Stop smoking</td>
</tr>
<tr>
<td></td>
<td>Weight loss</td>
</tr>
<tr>
<td></td>
<td>Decrease alcohol consumption</td>
</tr>
</tbody>
</table>

**Table 6. PASS (PPI Acid Suppression Symptom) test**¹⁵

1. Are you still experiencing GERD symptoms?
2. Are you taking any other medications to control your GERD symptoms: antacids, H2RAs, motility drug, or others?
3. Is your sleep affected by your heartburn?
4. Are your eating and drinking habits affected by your heartburn?
5. Does your heartburn interfere with your daily activities?

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1. 2009; 3: B.C. C.E.
2. www.canadianhealthcarenetwork.ca | pharmacy practice | November 2009 | B.C. CE 3
INITIAL TREATMENT
When treating moderate to severe GERD initial treatment should begin with once-daily PPIs. There is no significant difference seen in efficacy among the different PPIs when used in standard doses (Table 7). Although some studies have shown that double dose esomeprazole (40 mg twice daily) was found to result in a somewhat higher four- and eight-week healing rates when compared with standard dose omeprazole, pantoprazole, or lansoprazole in more severe disease, the clinical impact of this is debated. Results of these studies are not consistently replicated, so no recommendation has been made for preference of PPI in either initial or long-term treatment or in healing of esophagitis.

PERSISTENT SYMPTOMS
All patients should be reassessed after four to eight weeks of consistent treatment with once daily PPIs. Patient response is typically very positive by this point in therapy with healing rates for erosive esophagitis at four weeks being 66–81% and 75–95% at eight weeks. The number of patients who achieve complete resolution of heartburn-dominated dyspepsia has been shown to increase over time from four to 16 weeks of treatment. However, persistent symptoms after more than eight weeks of compliant therapy may require a “step-up” in the dosage to twice daily therapy since gastric acid suppression has been shown to be dose-related. Twice-daily therapy (double the daily dose) is considered to be more effective than giving double the dose once daily as it has been shown to prolong the increase in pH. Adjunctive treatment with H2RAs at night or use of prokinetic agents, such as domperidone or metoclopramide with or without H2RAs has not been shown to be effective in patients who have not responded adequately or at all to doubling of the PPI dose.

PPIs have demonstrated their clinical efficacy and safety in a number of trials, but despite this there are still a certain number of patients who are considered “non-responders.” This may be caused by non-compliance, a drug interaction that may interfere with PPI or H2RA, or their symptoms may not be due to GERD.

It is possible to explain the interindividual variability in response by looking at the differences in metabolic pathways and the prevalence of different types of metabolizers.

PPIs are extensively metabolized by CYP450 enzyme system, specifically CYP2C19. Patients may be extensive metabolizers or poor metabolizers, based on interindividual and interethnic variability in polymorphisms. For example, up to 23% of Asian Oceanian populations are poor metabolizers but only 1.2–3.8% of Caucasian Europeans are poor metabolizers. Extensive metabolizers, comprising most of the remaining percentage of the Caucasian population, will demonstrate a higher likelihood of therapeutic nonresponse since the clinical efficacy of PPIs depends on the extent and duration of gastric acid suppression. All the PPIs demonstrate some involvement of the CYP2C19 and CYP3A4 enzymes in their metabolism. Esomeprazole and rabeprazole are less dependent on 2C19 than are the other

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**Figure 1.**

Patient seeking medication for “Heartburn”

**SYMPTOMS**

- **FREQUENCY/SEVERITY/Effect on HRQL:**
  - Mild/infrequent ≤2X/WEEK Minimal effect on HRQL
  - Moderate/severe/ frequent >3X/WEEK Significant effect on HRQL

**PREDICTABILITY**

- **YES**
  - i.e. after eating a large meal, etc.
- **NO**
  - Symptoms don’t occur with any pattern

**RESPONSE**

- **YES**
  - Refer immediately to MD
- **NO**
  - Refer back to MD

**PPI once daily dosing**

- **YES to PASS test Question(s)**
  - Severe symptoms persist after 8 weeks
  - Continue current therapy
  - MD may consider “step-down” therapy or c/d medication to determine need
  - MD: Twice daily PPI, Switch PPI, further investigations

- **NO to PASS test Question(s)**
  - 4-8 weeks later
  - Consider alginates/antacids

**H2RAs – to be taken 30-60min prior to a meal or predicted heartburn/reflux**

**PHARMACIST INTERVENTIONS**

**PHYSICIAN INTERVENTIONS**

**HRQL**

**HEALTH RELATED QUALITY OF LIFE**
## Table 7. Medications available in Canada for the treatment of GERD

<table>
<thead>
<tr>
<th>Drug / trade names</th>
<th>Dose</th>
<th>Recommendations/common side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antacids: work by neutralizing stomach acid</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aluminum Hydroxide/Magnesium Hydroxide and various combinations may contain simethicone Available as liquid Examples: Maalox, Diovol</td>
<td>10–20 ml/dose qid PRN (max daily dose 80 ml of regular strength suspension)</td>
<td>Separate dosing from other medication by at least two hours to avoid interaction. Side effects: constipation, diarrhea Avoid in patients with renal insufficiency Taken after meals and at bedtime</td>
</tr>
<tr>
<td>Calcium Carbonate And combinations with magnesium hydroxide and or simethicone Available as suspension and tablets Examples: TUMS, Rolaids; Maalox tablets, Diovol Plus AF</td>
<td>10–20 ml or 2–4 tablets (max daily dose of 80 ml or 16 tablets regular strength products)</td>
<td>Separate dosing from other medications by at least two hours to avoid interaction. Side effects: constipation, diarrhea, nausea, Magnesium and aluminium containing products should be avoided in renal insufficiency Taken after meals and at bedtime</td>
</tr>
<tr>
<td><strong>Alginates: work non-systemically to form a foam barrier which floats on stomach contents that may protect the esophagus from gastric acid</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alginic acid/aluminum hydroxide Available as Examples: Gaviscon Liquid</td>
<td>10–20 ml when symptoms occur (max daily dose is 80 ml)</td>
<td>Separate dosing from other medications by at least two hours to avoid physical interaction. Side effects: nausea, vomiting, eructation, flatulence Contains sodium Safe for use during pregnancy</td>
</tr>
<tr>
<td>Alginic acid/magnesium carbonate Example: Gaviscon tablets</td>
<td>2–4 tablets chewed thoroughly when symptoms occur (max daily dose is 12 tablets) Follow with a glass of water</td>
<td>Separate dosing from other medications by at least two hours to avoid physical interaction. Side effects: nausea, vomiting, eructation, flatulence Contains sodium Safe for use during pregnancy</td>
</tr>
<tr>
<td><strong>H2RAs work by blocking H2 receptors in the parietal cell, to reduce acid production</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cimetidine Example: NU-CIMET</td>
<td>600 mg bid</td>
<td>Prevalence of CYP450 interactions limits its usefulness. Side effects: diarrhea, dizziness, rash, gynecomastia, headache, confusion (in elderly patients most likely due to decreased renal function)</td>
</tr>
<tr>
<td>Famotidine Example: Pepcid AC; Pepcid; Pepcid Complete (combination product with calcium carbonate and magnesium hydroxide)</td>
<td>10–20 mg bid</td>
<td>Not been shown to interact with medications metabolized by CYP450 enzymes Side effects: constipation, diarrhea</td>
</tr>
<tr>
<td>Nizatidine Example: AXID</td>
<td>150 mg bid</td>
<td>Not been shown to interact with medications metabolized by CYP450 enzymes Side effects: abdominal pain, diarrhea, nausea, headache</td>
</tr>
<tr>
<td>Ranitidine Example: Zantac 75; Zantac</td>
<td>75–150 mg bid</td>
<td>Not been shown to significantly affect metabolism of medications dependent on CYP450 enzymes Side effects: abdominal pain, constipation, diarrhea, nausea, vomiting, dizziness, fatigue, confusion, cardiac effects, rash</td>
</tr>
<tr>
<td><strong>Proton Pump Inhibitors: work by inhibiting the final common pathway for acid secretion</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omeprazole Example: Losec; Losec MUPS</td>
<td>20 mg once daily 30 minutes before breakfast or dinner</td>
<td>Recommended to: 1) give dose twice daily in non-responders or partial responders 2) halve dose for maintenance therapy when possible. Caution when combining with other medication metabolized by CYP450 enzymes. Side effects: Abdominal pain, diarrhea, headache</td>
</tr>
<tr>
<td>Rabeprazole Example: Pariet</td>
<td>20 mg once daily 30 minutes before breakfast or dinner</td>
<td>See recommendations and caution for omeprazole Side effects: Diarrhea, nausea, vomiting, constipation, headache</td>
</tr>
<tr>
<td>Pantoprazole Example: Pantoloc</td>
<td>40 mg once daily 30 minutes before breakfast or dinner</td>
<td>See recommendations and caution for omeprazole Side effects: headache, diarrhea, flatulence, abdominal pain</td>
</tr>
<tr>
<td>Lansoprazole Example: Prevacid; Prevacid FasTab</td>
<td>30 mg once daily 30 minutes before breakfast or dinner</td>
<td>See recommendations and caution for omeprazole Side effects: diarrhea, nausea, abdominal pain, headache, fatigue</td>
</tr>
<tr>
<td>Esomeprazole Example: Nexium</td>
<td>40 mg once daily 30 minutes before breakfast or dinner</td>
<td>See recommendations and caution for omeprazole Side effects: headache, diarrhea, nausea, flatulence, abdominal pain, constipation, and dry mouth</td>
</tr>
</tbody>
</table>
PPIs. Esomeprazole is predominantly metabolized by 3A4 and rabeprazole is dependent on non-enzymatic pathways. Recent studies have demonstrated that extensive metabolizers are at higher risk of recurrence during step-down maintenance therapy than patients who are average or poor metabolizers. Ideally, a dosage regimen based on genotype would improve outcome in these patients. There is currently a commercially available test for CYP2C19 genotyping, however the cost at $260 (U.S), from Genelex Corp., would not be covered by provincial insurance plans and would be too high for most patients. Since it is not possible to tell which patients are extensive metabolizers without testing, more aggressive therapy in patients who fail to respond to standard dosing may overcome this decrease in effectiveness. The proportion of patients who experience treatment success is lower among patients with ENRD (endoscopy-negative reflux disease) than patients with erosive esophagitis. This may indicate that those patients have other causes for their symptoms, such as functional heartburn.8

When patients are refilling a prescription for acid suppression therapy, pharmacists can administer the PASS test, a simple five-point questionnaire to assist in identifying those patients who would benefit from altering therapy. If patients answer positively to any of the five questions (Table 6), follow-up with their physicians should be recommended because they may require changes to their treatment.15

Long-term management

Because of the high likelihood of recurrence in the absence of maintenance therapy, many GERD patients will require a long-term management plan. To avoid unnecessary use of continuous long-term therapy, the ideal is to control patients’ symptoms and have a positive effect on their quality of life, with the lowest effective dose possible. Most patients will require some type of maintenance therapy.

In order to minimize unnecessary and prolonged acid suppression, patients who have responded well to standard therapy for GERD can discontinue their medication in an effort to determine if continued treatment is necessary. Some patients may relapse within a week, but others will not have symptom recurrence for six months or more. Of course, patients with more severe disease will likely have more difficulty in achieving remission; indeed, 70–100% of patients with esophagitis and 75% of patients with ENRD will relapse within six months.1

If, in as many cases, it is undesirable to discontinue medication completely, step-down therapy to a medication and a dose that continues to control the patient’s symptoms is the goal. Typically, treatments can include half treatment dose of PPIs, H2RAs, intermittent PPI therapy or on-demand PPI therapy, as long as the chosen treatment leads to symptom resolution. Patients with esophagitis are not likely to respond to H2RAs.1,8

Pharmacists can administer PASS test questions at prescription renewals and ensure that symptoms have not worsened or reoccurred and that alarm features are not present. Any issues will require further referral to their physician.

Continuous therapy

Although acid suppressive therapy should ideally not be used continuously, there are some patients in whom this would be necessary. Patients with erosive esophagitis will have difficulty with step-down therapy and may not have a complete response to double-dose PPI treatment. Often these patients add other OTC medications to their treatment.

Patients with esophageal ulceration, hemorrhage, stricture or Barrett’s esophagus, regardless of whether they have any symptoms of reflux, may also warrant continuous therapy with PPIs.1

Intermittent therapy

Intermittent therapy is used for patients with infrequent but severe recurrent GERD symptoms. This step-down treatment strategy refers to the administration of anti-secretory medication for a specified period of time (typically two to eight weeks but it can vary depending on the patient’s symptoms and responses) after the patient has had a relapse. Upon recurrence of symptoms, patients will take medication for a period of time specified by their physician. They can restart whenever a relapse occurs.1

On-demand therapy

This treatment strategy is used for patients with ENRD. Patients take their acid suppressive therapy until symptoms resolve and then discontinue their medication until a relapse occurs. This long-term, “patient-driven” management plan may be effective in up to 60% of patients requiring on-going treatment for GERD.1 Note that among the PPIs, esomeprazole 20 mg is currently the only one indicated for on-demand therapy in Canada.

Discontinuing medication

A recent double-blind placebo-controlled study has examined the incidence of rebound acid hypersecretion in healthy patients (no previous acid related disorder) after withdrawal of PPI therapy. In this study, over 40% of patients randomized to PPIs reported one or more “relevant, acid related symptom” after abrupt discontinuation of therapy.14 Few other studies have looked at tapering dosages of PPIs compared with stopping suddenly and failed to demonstrate a clinically significant difference.15 Having said that, anecdotal reports of tapering PPI doses over several weeks have been mentioned and may be useful in patients who have concerns about stopping suddenly or who have failed a previous attempt at abrupt discontinuation.36

Treatment of GERD in pregnancy

Heartburn is reported in 45–80% of pregnant patients and although it is self-limited, the amount of discomfort it can cause can be distressing.10 Typically, GERD arises as a new problem during pregnancy, worsens in the latter half of pregnancy and resolves shortly after delivery. The development of GERD during pregnancy is thought to be related to increased levels of hormones (progesterone), but it has also been linked anecdotally to the growth of the uterus.

Pregnant patients are often reluctant to use any medications during pregnancy due to the concern over the possible effects that they might have on the growing fetus. This concern is obviously well-founded since there is limited information on the use of many medications in pregnancy. The major risk to the fetus occurs during the first trimester when organogenesis is maximal. With this in mind, the treatment of GERD in pregnancy should begin with lifestyle modifications. According to the Canadian Dyspepsia working group, if these simple measures fail, antacids should be the first line of treatment.16 Products which contain calcium carbonate are preferred and can double as antacid and calcium supplement. Antacids which
contain sodium bicarbonate should be avoided since they can lead to metabolic alkalosis and fluid overload in both mother and fetus. Alginites, such as Gaviscon™, are considered safe for use during pregnancy. Although there is no published data regarding adverse effects of the use of antacids which contain aluminium and magnesium in pregnancy, theoretically, absorption of aluminium could affect developing organs in the fetus such as the brain and kidneys. Magnesium, in large quantities and ingested over prolonged periods of time, could lead to adverse outcomes such as nephrolithiasis and respiratory distress. Limiting the amount of products containing these active ingredients, combined with their low absorption, would likely be sufficient in eliminating the possible risk associated with their use.17

The next group of products that have been evaluated by meta-analysis of data by Motherisk are the H2RAs, the most commonly studied being ranitidine. A systematic review by the Motherisk Program (Hospital for Sick Children, Toronto, ON) showed no increased risk for fetal malformations or other complications (teratogenicity, increased risk of miscarriage or increased risk of low birth weight) when H2RAs are used during pregnancy.18 Failure of H2RAs and persistence of symptoms could call for referral to their physician and possibly for the use of a proton pump inhibitor. Another systematic review by the same group revealed no increased risk of major malformations in infants exposed to PPIs during gestation. The PPI that is the most commonly used and reviewed is omeprazole.16,18 Having said this, the U.S. FDA has assigned omeprazole to “category C” which is defined as “human data lacking; animal studies positive; or not performed.” This is due to animal studies that suggest toxicity to the fetus at high doses. In contrast, the FDA has assigned lansoprazole to “category B”, defined as “reassuring animal data”, despite the fact that it has not been as extensively used during pregnancy.16 Pharmacists should counsel pregnant patients to always use medications at the lowest effective dose and for the shortest period of time possible. Data on long-term outcome of prenatal exposure does not exist.

Side effects

Patients’ tolerance of medications is one of the prime indicators of their success in treating any condition. Pharmacists must be on the lookout for side effects that may affect patient compliance when determining the effectiveness of their treatment.

OTC medications typically are without any significant side effects due to the sporadic nature of their use. Antacids containing magnesium and aluminium should not be used in patients with renal insufficiency due to the potential for CNS depression (magnesium) and accumulation in brain and other tissues (aluminium). As well, magnesium/aluminium containing antacids may cause diarrhea and constipation.20

Though typically without significant side effects, H2RAs have the potential to cause the following: nausea, constipation, diarrhea, abdominal pain, headache, dizziness.20 (See Table 7 for more specific details) Serious side effects, such as cardiac conduction abnormalities, are rare and have been associated with rapid intravenous injection.21

PPIs, as a class, are generally well-tolerated medications. The most common side effects noted have been headache, diarrhea and abdominal pain, but these occur no more frequently with PPI use than with placebo.20

The continuous use of PPIs has been linked to several complications. Vitamin B12 deficiency, C. difficile infection, community-acquired pneumonia and increased risk of fractures have been associated with use of this class of medication. The studies, being observational, are not designed to implicate that these drugs cause any of the above side effects but have demonstrated an association, therefore the risk to the patient is uncertain.22–25 A review of the current literature reveals the following regarding adverse effects associated with long-term PPI usage:

- **B12 deficiency**: studies have produced mixed results. Routine levels not recommended until larger controlled trials have taken place.37
- **C. difficile**: studies have limited strength due to the retrospective designs and small numbers of patients. A systematic review of the topic did find an association between acid suppression therapy and an increased risk of enteric infection (pooled odds ratio 1.94; 95% CI, 1.37–2.75). The authors concluded that prospective trials are needed to determine causality.38
- **Pneumonia**: data are not conclusive. A 2009 UK population based case control study demonstrated an increased risk of community-acquired pneumonia (adjusted odds ratio of 1.55; 95% CI, 1.38–1.77).39 In clinical practice it would be prudent to use cautious when administering PPIs to patients who may be at risk for pneumonias (elderly patients with chronic lung disease on immunosuppressant medication and patients with recurrent respiratory infections).
- **Increased risk of fractures**: evidence is not conclusive. PPIs are believed to affect the absorption of calcium from the gut. A recent case control study has shown an increased incidence of osteoporosis related fractures after five or more years of exposure (adjusted OR 1.92, 95% CI 1.16–3.18).40 No prospective trials have been conducted, therefore screening for osteoporosis cannot be recommended at this point, however it is widely acknowledged that more information about the effects of PPI therapy on calcium absorption is needed.37

With all this in mind, as pharmacists, we must discuss with patients any adverse effects that they are experiencing and provide feedback to the prescribing physician and to Health Canada when necessary.

Drug interactions

There is a definite role for pharmacists in the avoidance of drug interactions and informing patients of the potential for drug interactions when they are being treated for GERD.

The most obvious interactions are with the over-the-counter antacids that are commonly chosen by patients when seeking relief for heartburn. Aluminum- and magnesium-containing antacid products can chelate and interfere with the absorption of various medications when administered concomitantly These include ASA, azithromycin, biphosphonates, DDI (didanosine), quinolones and tetracycline. It is recommended that antacids not be given at the same time as other medications (separate dosing by 1–2 hours).20

H2RAs, such as ranitidine, famotidine and nizatidine, are, on the whole, without significant drug interactions. The exception in this class of drugs is cimetidine, which is not as commonly used due to its potential for clinically significant drug interactions. Through inhibition of CYP450 enzyme systems, cimetidine can reduce the hepatic metabolism of medications including warfarin-type anticoagulants, phenytoin, propranolol, nifedipine, diazepam, tricyclic antidepressants, lidocaine, theophylline and metronidazole. In decreasing the elimination of these agents, elevated levels of these drugs have the ability to cause some significant adverse effects. It is recommended to avoid the use of cimetidine whenever possible in these patients. If not possible,
close monitoring and dose adjustment when necessary is advised.

All H2RAs have the potential to interfere with the absorption of drugs dependent on low gastric pH, such as ketoconazole. 20

PPIs may interact with other medications via several different mechanisms. First, the increase of gastric pH may alter the absorption of various drugs or modify their release from their dosage forms. 1 Increased absorption and elevated drug levels can lead to toxicity of digoxin, furosemide, cyclosporine and ASA when these agents are given with PPIs. Co-administration of PPIs can lead to decreased absorption and therefore decreased efficacy of ketoconazole.

Secondly, PPIs can affect both first-pass metabolism and hepatic clearance through the cytochrome P450 enzyme system of various drugs. All PPIs are metabolized via CYP2C19, and to a lesser extent 3A4, some more extensively than others. In vitro studies have shown that all PPIs demonstrate competitive inhibition of 2C19. 26

Some potentially clinically significant drug interactions may occur when PPIs are used together with simvastatin, diazepam, warfarin and phenytoin where increased drug levels can result. In addition, poor metabolizers that lack 2C19 may be particularly predisposed. 27 St. John's wort has been shown to decrease the serum concentration of omeprazole. 28

Recently, two studies have examined the effect of PPIs on the metabolism of clopidogrel. These observational studies have shown a decrease in the antiplatelet effect of clopidogrel and increased risk of cardiac events when it is given together with a PPI. These data suggest that omeprazole inhibits CYP2C19 to the greatest extent and is associated with a higher degree of clopidogrel failure. 29, 30 A third, more recent analysis of two studies did not find an association between the use of PPIs and decreased efficacy of either clopidogrel or prasugrel or adverse cardiac outcomes. Though this is reassuring, only a randomized trial will provide definitive evidence regarding the safety of the concomitant use of these medications. 31 At this point, pharmacists should ensure that patients are being treated appropriately and with clear indication for the combination, i.e., increased risk of GI bleed. No recent consensus statement has been issued since the newer studies were published.

**Summary**

Pharmacists assisting patients in their management of GERD should remember to let the patients’ symptoms dictate the type of treatment required. The presence of alarm features will require immediate referral to their physicians. Mild and infrequent GERD can most often be treated with OTC medication such as antacids, alginites or H2RAs taking the whole patient into consideration. For instance, consider whether the patient is elderly with possible renal insufficiency or is a pregnant woman experiencing the common symptom of heartburn. We need to be able to help these patients make decisions that will lead to the safest and most effective choice possible.

Moderate or severe GERD will require pharmacists to initially refer patients to their physicians for treatment. Being vigilant in our continued management of prescription renewals by asking patients to describe any ongoing symptoms, and by administering the PASS questionnaire, will allow us to identify patients who require changes in their treatment, such as a step-up to double the daily dose of PPI or a step-down to intermittent or on-demand therapy when indicated.

Patients who suffer from GERD often go it alone and self-medicate without the input of a health professional. A significant contribution to the care of patients with GERD is possible for pharmacists when we are proactive and become comfortable in our knowledge of treatment options.

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**BC Case Study**

**Prescription adaptation by pharmacists in BC**

The BC government’s 2008 Health Professions (Regulatory Reform) Amendment Act formalizes a pharmacist’s authority to “renew existing prescriptions.” The College of Pharmacists of British Columbia (CPBC) developed Professional Practice Policy #58 (PPP-58), entitled “Protocol for Medication Management – Adapting a Prescription,” to guide pharmacists in the context of effective adaptation, including renewal, of existing prescriptions. This policy took effect January 1st, 2009. (See College of Pharmacists of British Columbia. Professional Practice Policy #58 Orientation Guide: Medication Management [Adapting a Prescription]). Pharmacists in BC have the authority to adapt prescriptions without prior approval from the prescriber; however, they are not obligated to do so. The decision to adapt or not to adapt a prescription is at the discretion of the individual pharmacist. Once a pharmacist adapts a prescription, they assume responsibility and liability, for that prescription. PPP-58 sets out seven fundamental elements that must be fulfilled when adapting a prescription:

- Individual competence
- Appropriate information
- Prescription
- Appropriateness of prescription
- Informed consent
- Documentation
- Notification of other health professionals

Details on each of these elements can be found in the CPBC’s Orientation Guide for PPP-58.

**Types of adaptation**

The current scope of practice in BC specifies three professional activities as adapting a prescription:

- Changing the dose, formulation or regimen of a prescription to enhance patient outcomes;
- Renewing a prescription for continuity of care; and
- Making a therapeutic substitution within the same therapeutic class for a prescription to best suit the needs of the patient.

Details on the three types of prescription adaptation can be found in the College of Pharmacists of BC’s Orientation Guide for PPP-58 and the Amendment to the Orientation Guide. It is important to be aware of the specific requirements around the three types of adaptation, for example, renewals apply only to stable, chronic conditions for which the patient has taken the same medication for at least six months. As well, changes to dose or regimen and therapeutic substitutions are restricted to specific conditions or classes of drug unless the pharmacist is in a practice setting where collaborative relationships or appropriate protocols are established.

Pharmacists cannot adapt a prescription if the original prescription has expired (one year from the date the original prescription was written, or two years for oral contraceptives). Pharmacists also cannot adapt a prescription for narcotic, controlled drugs or targeted substances.
CASE STUDY

This case study is an example of a scenario that could occur in a community pharmacy. It illustrates how pharmacists can play a role in helping their patients manage a condition such as GERD. In an effort to ensure an optimal patient outcome, the pharmacist may decide to adapt a prescription. This decision must follow the seven fundamental elements outlined in PPP-58. The intention of this case is to examine how a pharmacist may handle a specific situation involving a specific patient. It is not the intention of this case study to imply that all pharmacists should adapt a prescription in this manner or that it would be appropriate for all situations.

Forty-year-old Gordon, a regular patient in your pharmacy, arrives to pick up a prescription for omeprazole 20 mg daily. Previously, Gordon had used whatever antacids he had on hand to relieve his symptoms of GERD. He has been using these products off and on for the past few months but lately his symptoms have worsened. Gordon confides that he doesn’t understand why his symptoms are getting worse and that his doctor suggested that he talk to you about some lifestyle changes. You work closely with his doctor and have established a good working relationship with him, so this request is not a surprise. You tell Gordon that changes to one’s food and lifestyle habits sometimes help with symptoms.

Gordon says he is 5’9” and weighs 190 lbs; you calculate his BMI to be 28 Kg/m². He tells you that he has gained some weight over the last few months because of his new position. He has an office job and likes to eat out quite a bit, especially at greasy spoons. He does not smoke but “lives on coffee.” His idea of relaxing is having a few beers with his buddies while watching sports on television. When you ask if any particular foods or beverages seem to trigger his symptoms, he reluctantly admits that spicy foods really cause a burn.

You realize that Gordon may benefit from a few lifestyle interventions (see Table 5). You make the following suggestions: lose some weight, eat smaller meals, avoid wearing tight clothing, limit his alcohol and coffee intake, and avoid spicy and fatty foods. You also suggest Gordon keep a food diary.

You ask him how confident he would be about making these changes. He says some would be fairly easy, but he’s not sure if he’s ready to cut back on coffee and alcohol. You agree that it would be a lot to change at once so you ask him what changes he would be willing to commit to. He agrees to eat smaller meals and to limit his alcohol intake to no more than two drinks per day. He will also try to go to the gym once a week. It’s a great start and you tell him so. But you also explain to him that, even with the suggested lifestyle changes, his symptoms may persist, but to a lesser degree. Gordon understands, but says his physician told him his symptoms could get worse over time and he would like to prevent that.

Nine weeks later, Gordon returns with a new prescription for pantoprazole 40 mg daily. He had been experiencing inadequate symptom relief so his physician decided to try him on this medication. Gordon’s doctor has encouraged him to continue working with you on his lifestyle changes. You ask Gordon about his progress and he says he made all the changes the two of you had discussed. The food diary has helped him be more aware of—and avoid—the foods that bother him. After some discussion, Gordon agrees to limit his coffee to no more than three cups a day—four, tops! He has a follow-up appointment with his doctor in four weeks and promises to let you know how it goes.

Gordon returns four weeks later with a prescription to refill his pantoprazole. He tells you the medication seems to be working and says he’s managed to reduce his coffee intake to three cups a day and he’s even playing soccer regularly. You congratulate him and encourage him to continue with his changes.

About six months later Gordon returns with a refill prescription for pantoprazole. He explains that will be away for business for the next six weeks and would like to get a two-month supply instead of the usual four weeks. The prescription is written for a four-week supply, it is Saturday afternoon and Gordon will be leaving the next day. During your discussion, you administer the PASS test15 and Gordon reports satisfactory symptom relief.

In the interest of continuity of care, you explain to Gordon that you can adapt the prescription and dispense an eight-week supply. You also tell him that you will fax his doctor to let him know of this change. Gordon agrees.

Two months later, Gordon has run out of his medication. He was unable to keep his last doctor’s appointment and he is leaving town again. You proceed with an assessment. You determine that he is not experiencing any alarm symptoms but this time his PASS test is positive: his sleep has been affected by his heartburn, especially when he is away on business. After reviewing the seven fundamentals of adapting a prescription, as defined by PPP-58, you decide to adapt Gordon’s prescription by making a therapeutic substitution. You explain to Gordon that his present therapy regimen is not effective and suggest an alternative PPI, esomeprazole 40 mg once daily. As with your earlier adaptation to ensure continuity of care, in reaching this decision you meet the seven fundamentals of adaptation:

Individual competence – You have adequate understanding of the condition being treated, treatment alternatives and the drug being prescribed. You are familiar with the Practice Guidelines prepared by the Canadian Consensus Conference on the management of gastroesophageal reflux disease.

Appropriate information – You have enough information about the specific patient’s health status to ensure that the prescribing decision will maintain or enhance the effectiveness of the drug therapy and will not put the client at increased risk. You have assessed the patient and feel comfortable that the client has shared all pertinent information available with you.

Prescription – You have the original prescription for pantoprazole.

Appropriateness of adaptation – According to the PPP-58 amendments, “unless in practice settings such as hospital, long-term care facilities or multi-disciplinary environments where collaborative relationships or appropriate protocols are established, pharmacists will limit therapeutic substitution to: histamine 2 receptor blockers (H2 blockers), non-steroidal anti-inflammatory drugs (NSAIDs), nitrates, angiotension converting enzyme inhibitors (ACE inhibitors), dihydropyridine calcium channel blockers (dihydropyridine CCBs) and proton pump inhibitors (PPIs)—similar to government policies.”

Esomeprazole is a proton pump inhibitor and is indicated for treatment of conditions where a reduction in gastric secretion is required, such as reflux esophagitis and maintenance treatment of patients with reflux esophagitis. Reflux symptom improvements in PASS study results were associated with a switch to esomeprazole 40 mg daily from another PPI. Esomeprazole at a dose of 40 mg daily produces more prolonged acid suppression than standard doses of the four other PPIs available in Canada and is associated with somewhat higher healing rates than omeprazole, lansoprazole, and pantoprazole for patients
with erosive esophagitis.

Informed consent – Before adapting, you must obtain the voluntary consent of the patient. The patient must have the capacity to consent. A patient has the right to be adequately informed before consenting to treatment, so it is important the patient has sufficient information to allow them to reach an informed decision. You have explained to Gordon your authority to make a therapeutic substitution and have given him the opportunity to ask any questions and have ensured he understands the discussion. You ask if he would like you to make a substitution. He indicates his consent by answering yes.

Documentation – You complete the documentation required by filling out the entire form available from the College of Pharmacists of BC (www.bcparmacists.org). See Figure 2.

Notification – You fax the completed form to Gordon's doctor within 24 hours of adapting the prescription.

Case conclusion

Satisfied that you have met the criteria for adaptation, you dispense a four-week supply of esomeprazole. You inform Gordon that you will contact his doctor about the change and ask him to book an appointment with his doctor when he gets back. You also encourage him to continue his nonprescription and lifestyle measures. Three weeks later, during a scheduled call back with Gordon, he informs you that he will be bringing in a new prescription for the esomeprazole. You inform Gordon that you will contact his doctor about the change and ask him to book an appointment with his doctor when he gets back. You also encourage him to continue his nonprescription and lifestyle measures. Three weeks later, during a scheduled call back with Gordon, he informs you that he will be bringing in a new prescription for the esomeprazole in the next few days.

Figure 2.

Pharmacist Prescription Adaptation Documentation and Notification Form

<table>
<thead>
<tr>
<th>Patient Information</th>
<th>Pharmacist Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name: Gordon B.</td>
<td>Name: Jones Pharmacy</td>
</tr>
<tr>
<td>PHN: 123-4567</td>
<td>Phone: 604-987-1234</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Prescriber Information</th>
<th>Date of Notification:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name: Dr. John Smith</td>
<td>November 8, 2009</td>
</tr>
<tr>
<td>Phone: 604-123-4567</td>
<td></td>
</tr>
<tr>
<td>Fax: 604-123-5678</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Original Prescription Information</th>
<th>Details:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date: July 15, 2009</td>
<td>Esomeprazole 40 mg once daily x 28 days</td>
</tr>
<tr>
<td>Details: Pantoprazole 40 mg once daily x 28 days</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Rationale for Adaptation (Including Instructions to Patient and Follow-up Plan)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rationale: Gordon initially requested a removal of pantoprazole for continuity of care. However, he failed the PASS Test. While not exhibiting alarm symptoms, he reported right side awakenings with GERD symptoms.</td>
</tr>
<tr>
<td>Instructions to Patient: Asked patient to book appointment with physician within four weeks.</td>
</tr>
<tr>
<td>Follow-up Plan: Scheduled a pharmacy call-back in three weeks.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Informed Consent</th>
</tr>
</thead>
<tbody>
<tr>
<td>The patient and/or their representative (name: Gordon B.) was provided sufficient information, including the risks and benefits associated with the adaptation and voluntarily provided their consent.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Notification Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of Notification: November 8, 2009</td>
</tr>
<tr>
<td>Name of Practitioner(s) Notified: Dr. John Smith</td>
</tr>
<tr>
<td>Method of Notification (fax preferred):</td>
</tr>
<tr>
<td>✅ Fax # 604-987-1234</td>
</tr>
</tbody>
</table>

1. Approximately what proportion of Canadians report experiencing heartburn in the last three months?
   a) 2–5%
   b) 10–20%
   c) 40–50%
   d) 75%

2. The cause of reflux is most likely due to:
   a) eating spicy food
   b) being overweight
   c) an increase in transient LES relaxations
   d) smoking

3. Which of the following is NOT a risk factor for developing GERD?
   a) smoking
   b) being female
   c) pregnancy
   d) anxiety or depression

4. Which of the following medications may cause GERD?
   a) acetylsalicylic acid
   b) oxygen
   c) warfarin
   d) salbutamol
   e) b and d

5. Which of the following would lead to a diagnosis of GERD by a pharmacist?
   a) regurgitation
   b) solid food dysphagia
   c) burning sensation beneath the breast bone that may rise to the back of the throat
   d) chest pain
   e) a and c

6. Which of the following is NOT considered an alarm feature?
   a) nocturnal heartburn
   b) odynophagia
   c) chest pain
   d) gastrointestinal bleeding
   e) vomiting

7. Patients with mild disease:
   a) experience only heartburn at night
   b) experience symptoms ≤ 2 times per week
   c) experience symptoms 3 times per week
   d) experience heartburn once daily

8. Indications for long-term GERD treatment include all of the following except:
   a) esophageal strictures
   b) chronic cough
   c) erosive esophagitis
   d) esophageal ulceration
9. The best choice for treatment of patients with mild GERD with predictable symptoms is:
   a) TUMS
   b) ranitidine 30–60 minutes prior to trigger event (e.g., large meal)
   c) avoid lying down after the meal

10. Approximately what percentage of pregnant patients entering your pharmacy will experience GERD?
   a) 10–15%
   b) 25–30%
   c) 45–80%
   d) 90%

11. Which of the following statements about the treatment of GERD during pregnancy is most accurate?
   a) First-line treatment should be H2RAs since most patients don’t respond to antacids.
   b) Pharmacists should always suggest using the lowest effective dose possible for the shortest period of time possible.
   c) Health Canada states that PPIs are safe and effective in pregnancy.
   d) Patients should be referred to their physician for treatment.

12. When treating moderate to severe GERD the physician will often
   a) order an endoscopy
   b) begin with twice-daily PPI therapy
   c) order an H2RA blocker first to determine if this is sufficient for the patient
   d) begin treatment with a once-daily PPI
   e) advise patients to begin treatment with antacids

13. Patients started on PPI therapy should be reassessed after:
   a) two weeks
   b) six months
   c) four to eight weeks
   d) one week

14. Patients who have responded well to standard treatment for GERD can discontinue their medication to see if continued therapy is warranted.
   a) true
   b) false

15. Intermittent therapy is step-down therapy used for patients with frequent severe GERD to control symptoms without being on continuous therapy.
   a) true
   b) false

16. Which of the following statements about PPI side effects is most accurate?
   a) PPI use can cause C. difficile infection in up to 20% of patients.
   b) PPI use can cause pneumonia in 45% of elderly patients with underlying respiratory conditions.
   c) The risk of side effects with PPI use is low.
   d) When PPIs are compared with placebo, headaches occur more frequently in patients on PPIs than in patients on placebo.

17. The H2RA associated with the most significant drug interactions due to inhibition of CYP450 enzymes is:
   a) ranitidine
   b) cimetidine
   c) nizatidine
   d) lamotidine

18. All PPIs have demonstrated competitive inhibition of the following CYP450 enzyme:
   a) 3A4
   b) 2C9
   c) 2C19
   d) 2D6
   e) none

19. On PPI prescription renewal, which of the following questions are the most important to ask?
   a) Are you still experiencing heartburn?
   b) Are you taking any other medications for heartburn?
   c) Do your symptoms affect your sleep?
   d) All of the above
   e) a and c

20. Which of the following statements about PPI superiority over H2RAs in the treatment of GERD is inaccurate:
   a) Patients do not exhibit tachyphylaxis to PPI effects on acid suppression.
   b) PPIs have been shown to heal esophagitis faster.
   c) PPIs have a longer duration of action.
   d) PPIs have fewer side effects.
   e) PPIs are more effective at keeping gastric pH above 4 for longer periods of time.

21. The seven fundamentals of adaptation in BC are: individual competence, appropriate information, prescription, appropriateness of adaptation, education, documentation and notification of other health professionals.
   a) true
   b) false

22. When notifying other health professionals of an adaptation which of the following does not need to be included:
   a) patient information and pharmacist information
   b) description of the adaptation (including all relevant prescription details)
   c) rationale for adaptation (including pertinent details of your assessment and patient history along with any directions to the patient and relevant follow-up plan)
   d) patient medication profile
   e) acknowledgment of informed consent

23. When making a therapeutic drug substitution within the same therapeutic class, which of the following conditions must be met?
   a) The decision is in the best interest of the patient.
   b) You maintain your professional independence and avoid any conflict of interest.
   c) You have considered all relevant information about the patient, the condition and the medication and have communicated this to the patient and have received their consent for the substitution.
   d) You take full responsibility for your decision.
   e) The medication falls into one of the following drug classes: H2 blockers, NSAIDs, nitrates, ACE Inhibitors, dihydropyridine CCBs or PPIs
   f) All of above

24. In BC, which of the following medications would be allowed under PPP-58?
   a) esomeprazole
   b) captopril
   c) lorazepam
   d) a and b
   e) all of the above

25. Which of the following is not considered an adaptation?
   a) changing the dose, formulation or regimen of a prescription to enhance patient outcomes
   b) renewing a prescription for continuity of care
   c) making a therapeutic substitution within the same therapeutic class for a prescription to best suit the needs of the patient
   d) none of the above
References, main lesson


References, BC case study


About the authors

Norma Marchetti is a Drug Information Pharmacist at the Hamilton Health Sciences Centre in Ontario. She is also the co-author of the Pharmacist Specific Guidelines for Management of GERD with Dr. David Armstrong.

Livia Chan is a community pharmacist who has been practicing for 13 years. She currently adapts prescriptions in the practice setting and brings a grassroots experience to the topic of prescription adaptation in BC.

Reviewers

All lessons are reviewed by pharmacists for accuracy, currency and relevance to current pharmacy practice.

Continuing education project manager

Sheila McGovern, Toronto, Ont.
email: sheila.mcgovern@rogers.com

This lesson is valid until October 27, 2012. Readers are responsible for determining the most current aspects of this topic.

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Mayra Ramos
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More CCCEP-approved CEs or Tech Talk CEs (English and French)
Fax: (416) 764-3937
Email: mayra.ramos@rci.rogers.com

Francine Beauchamp
Quebec Pharmacie and L’actualite Pharmaceutique
Fax: (514) 843-2183
Email: francine.beauchamp@rci.rogers.com