Role of Low-Dose OTC PPIs for Frequent Heartburn Management

Each month, up to 44% of Americans experience at least 1 episode of heartburn, with approximately 70 million Americans experiencing frequent heartburn symptoms (2 or more days per week).1 4 Lifestyle modifications are helpful in reducing symptoms in some individuals, but many patients continue to experience frequent heartburn and may benefit from treatment with an OTC proton pump inhibitor (PPI).5,6 Pharmacists can help patients better understand the risks and benefits of various treatment options for frequent heartburn, including the appropriate use of a PPI at the lowest effective dose.

Heartburn occurs as a result of gastric acid flowing from the stomach into the esophagus, causing irritation that often manifests as a burning sensation in the chest. The severity of heartburn symptoms can vary considerably and, based on symptom frequency, heartburn may be classified as episodic (≤1 day per week) or frequent (≥2 days per week). Episodic heartburn is usually mild and may be triggered by lifestyle factors (eg, acidic/high-fat foods, alcoholic beverages, and smoking). By contrast, frequent heartburn occurring 2 or more days per week is considered bothersome by most patients.5

Comparing the Efficacy: Low-Dose Versus High-Dose PPIs
Nonprescription H2-receptor antagonists and inorganic antacids are appropriate for on-demand therapy in patients with episodic and meal-provoked heartburn. PPIs are appropriate as initial treatment for frequent heartburn, are clinically effective, and generally well tolerated.5 6 Although some PPIs are available by prescription only (omeprazole, pantoprazole, and dexlansoprazole), lower-dose options can be found over the counter. The first PPI to switch to OTC status was 20-mg omeprazole, marketed as Prilosec OTC (omeprazole magnesium).7 Other PPIs have since become available over the counter (eg, omeprazole/sodium bicarbonate and lansoprazole).5,8 10 Evidence has shown that OTC doses of PPIs can reduce heartburn symptoms within the first 1 to 4 days of a 14-day treatment and can provide sustained efficacy for the remainder of the treatment period.8 10

Higher doses of PPIs are associated with greater gastric acid suppression. Armstrong et al conducted a study to test the hypothesis that the greater acid suppression produced by esomeprazole would produce heartburn relief in a greater proportion of patients than omeprazole after 4 weeks of therapy. The results showed, however, that greater acid suppression may not correlate with more effective symptom relief in patients with endoscopy-negative reflux disease. In these 3 large multinational, double-blind, randomized, parallel-group multicenter studies, Armstrong et al evaluated the comparative efficacy of omeprazole (20 mg) and esomeprazole (20 mg or 40 mg) in reducing heartburn symptoms in patients with nonerosive gastroesophageal reflux disease, as determined by an endoscopic examination (Text Box). Participants were aged 18 to 80 years and reported having symptoms at least 4 days per week for at least 6 months at baseline.11

The primary end point of the trials was the percentage of patients experiencing complete resolution of heartburn at the end of the 4-week treatment period (28 ± 4 days), defined as patients reporting no symptoms in the past week. A secondary outcome was complete resolution of heartburn at the end of 2 weeks (14 ± 2 days).11

The results showed that the 20-mg dose of omeprazole was comparable to the 40-mg dose of esomeprazole in heartburn relief. There were no significant differences in rate of heartburn resolution at 2 weeks or 4 weeks between any of the treatments across the 3 studies (see Figure for 2-week results).11

Rationale for Using the Lowest Effective Dose
The lack of demonstrated superiority of higher doses compared with lower doses of PPIs in the symptomatic relief of heartburn11 suggests that OTC doses are appropriate for the treatment of frequent heartburn. Clinical experts as well as professional organizations such as the American College of Gastroenterology and American Gastroenterological

**TEXT BOX: ESOMEPRAZOLE VERSUS OMEPRAZOLE STUDY TREATMENTS**

<table>
<thead>
<tr>
<th>Study A</th>
<th>Esomeprazole 40 mg (n = 425)</th>
<th>Omeprazole 20 mg (n = 423)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study B</td>
<td>Esomeprazole 40 mg (n = 347)</td>
<td>Omeprazole 20 mg (n = 346)</td>
</tr>
<tr>
<td>Study C</td>
<td>Esomeprazole 20 mg (n = 336)</td>
<td>Omeprazole 20 mg (n = 334)</td>
</tr>
</tbody>
</table>
Association recommend, once healing has occurred, titrating PPI dosage down to the lowest effective dose for the shortest duration to control symptoms. Similarly, the FDA advises health care professionals to “consider whether a lower dose or shorter duration of therapy would adequately treat the patient’s condition.”

Role of the Pharmacist
Pharmacists play an important role in helping patients identify whether their symptoms are consistent with frequent heartburn and in counseling them on the appropriate use of an OTC PPI when treatment is indicated. Patients with alarm symptoms (gastrointestinal bleeding, nausea/vomiting, dysphagia, odynophagia, or weight loss) should be referred immediately for further evaluation. Patients with chronic cough, laryngitis, or asthma may require further diagnostic testing.

Pharmacists should counsel patients with frequent heartburn on lifestyle modifications, such as weight loss, dietary modifications, and avoiding late meals. When recommending a PPI, it is important for pharmacists to educate patients on the availability of OTC lower-dose options, which may offer results comparable to those of a higher-dose option that is only available by prescription. Guidelines recommend the lowest effective dose over the shortest duration necessary to control symptoms.

Patients should be instructed that PPIs be taken in the morning, 30 minutes to 1 hour before the first meal of the day (when gastric acid secretion levels are lowest), with a full glass of water. Patients who do not respond after 14 days of treatment should be referred to a physician for further evaluation.

Questions to Help Characterize Heartburn Symptoms

- When and how often does the pain occur?
- Where does the pain occur?
- Do certain foods exacerbate the pain?
- Does the pain worsen with physical activity?
- Are there any other symptoms associated with the pain?

References
7. Prescription to over-the-counter (OTC) switch list. FDA website. www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsand-