



June 12, 2002

Food and Drug Administration  
Center for Drug Evaluation and Research (HFD-21)  
ATTN: Sandra Titus  
5630 Fishers Lane  
Rockville, MD 20857

Dear Sandra:

I am Robert Seidman, Chief Pharmacy Officer of WellPoint Health Networks. WellPoint provides health care coverage to 13 million Americans nationwide through a portfolio of products designed to place individuals in control of their health and financial future. WellPoint, in its desire to provide access to an affordable prescription drug benefit, supports the new drug application (NDA) 21-229, proposing over-the-counter (OTC) use of PRILOSEC1 (omeprazole magnesium), AstraZeneca LP/Procter and Gamble, for the prevention of the symptoms of frequent heartburn.

More Americans than ever before are using OTC medicines for symptom relief of common ailments, such as heartburn. Today, three in five Americans (59%) report having taken an OTC drug in the past six months. Of the OTC drugs consumed, 37% are for heartburn, indigestion and other stomach problems<sup>1</sup>. Heartburn amongst Americans is a common complaint and more than 60 million American adults experience heartburn at least once a month<sup>2</sup>. Most people who suffer from heartburn usually seek self-treatment options such as antacids and histamine H-2 receptor antagonists, seeking the care of a physician when their symptoms persist.

The currently available OTC therapies provide only partial relief for many heartburn sufferers. Heartburn relief from antacids is usually prompt but short lived, requiring frequent administration, making nighttime relief of heartburn symptoms problematic. Histamine H-2 receptor antagonists have a much longer duration of action than antacids (up to 10 hours), but are less effective and long lasting than the current gold standard — Proton Pump Inhibitors. The FDA approval of prescription Proton Pump Inhibitors has revolutionized the treatment of heartburn and gastroesophageal reflux disease (GERD), providing relief to many who found earlier generations of drug therapy ineffective. There are now five Proton Pump Inhibitors approved by the FDA for the prescription treatment or symptomatic relief of various gastric disorders including gastric and duodenal ulcers, GERD, or pathological hypersecretory conditions. We believe that the safety and efficacy profiles of Proton Pump Inhibitors warrant the addition of Prilosec<sup>®</sup> (omeprazole) to OTC status for the symptomatic prevention of heartburn.

Antacids and OTC strength histamine H-2 receptor antagonists are currently the mainstay of therapy for initial patient-directed therapy for heartburn, but the current OTC drugs available do not prevent heartburn symptoms over a 24 hour period. Over-the-counter Prilosec<sup>®</sup> (omeprazole), in the 20mg dosage and with proper labeling and packaging, can provide heartburn sufferers with

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<sup>1</sup> Attitudes and Beliefs About the Use of Over-the-Counter Medicines: A Dose of Reality. A National Survey of Consumers and Health Professionals. Prepared for: National Council on Patient Information and Education (NCPPIE), January 2002  
<sup>2</sup> National Digestive Disease information Clearinghouse. Gastroesophageal Reflux Disease (Hiatal Hernia and Heartburn). Available at: <http://www.niddk.nih.gov/health/digest/pubs/heartbrn/heartbrn.htm>

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ready and easy access to the most effective agent for the prevention of frequent heartburn symptoms.

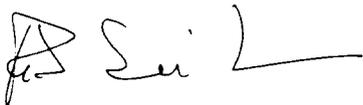
More than 10 million patients have taken Prilosec® (omeprazole) safely, the first FDA approved Proton Pump Inhibitor, in more than 450 million courses of therapy. Thousands of clinical studies have also been performed on Proton Pump Inhibitors documenting their safety and efficacy. Adverse effects from Proton Pump Inhibitors can include headache, dizziness, somnolence, nausea and diarrhea or constipation<sup>3</sup>, but these side effects are also usually mild and self limiting<sup>4</sup>. In reviewing the incidence of adverse effects from Proton Pump Inhibitors and histamine H-2 receptor antagonists, they appear similar<sup>3</sup>. Use of OTC Proton Pump Inhibitors in pregnancy and lactation are not recommended due to a lack of safety data in these patient populations, and this can be clearly referenced in the labeling for any OTC Prilosec® (omeprazole)<sup>5</sup>. From a drug interaction perspective, the Proton Pump Inhibitors are metabolized extensively, primarily by cytochrome P-450 2C19 and 3A<sup>6</sup>. These enzymes can metabolize other drugs, which theoretically could interact with Proton Pump Inhibitors, but few clinically important drug interactions have been reported<sup>4</sup>. Potential drug interactions with Prilosec® (omeprazole) that are found by the FDA to be significant can be adequately described in the over-the-counter labeling.

It is appropriate to ask whether Proton Pump Inhibitors could potentially mask a more significant medical event. In an OTC setting, self-treating patients should seek the guidance of a physician if a short course treatment regimen of Prilosec® (omeprazole) does not relieve their heartburn or they have the following symptoms<sup>7</sup>:

- Dysphagia
- Bleeding (i.e. coughing up blood)
- Unexplained weight loss
- Unexplained chest pain
- Choking (a sensation of acid reflux into the airways, causing coughing, shortness of breath, or hoarseness)

We believe that these warnings can be adequately displayed in the OTC labeling of Prilosec® (omeprazole) and that consumers would comprehend the importance of seeking physician directed care when necessary. Based on the many years of safe Prilosec® (omeprazole) use as a prescription drug, please provide the millions of Americans who suffer from uncomplicated heartburn access to Prilosec® (omeprazole) over-the-counter.

Thank you for your consideration in this matter.



Robert Seidman, Pharm.D., M.P.H.

<sup>3</sup> Williams DB. Gastroesophageal Reflux Disease. In: DiPiro JT, Talbert RL, Yess GC, et al, eds. Pharmacotherapy: A Pathophysiologic Approach. 4<sup>th</sup> ed. Stamford, CT: Appleton & Lange; 1999:532-47

<sup>4</sup> Welage LS, Berarsi RR. Evaluation of Omeprazole, Lansoprazole, Pantoprazole, and Rabeprazole in the Treatment of Acid-Related Disorders. J Am Pharm Assoc. 2000;40:52-62

<sup>5</sup> Broussard CN, Richter JE. Treating Gastro-Oesophageal Reflux Disease During Pregnancy and Lactation: What Are the Safest Therapy Options? Drug Saf. 1998; 19:325-37

<sup>6</sup> Garnett WR. Considerations for Long-Term Use of Proton Pump Inhibitors. Am J Health Syst Pharm. 1998;55:2268-79

<sup>7</sup> DeVault KR, Castell DO. Updated Guidelines for the Diagnosis and Treatment of Gastroesophageal Reflux Disease. AM J Gastroenterol. 1999;94:1434-42