NATIONAL PBM BULLETIN

April 3, 2007

DEPARTMENT OF VETERANS AFFAIRS VETERANS HEALTH ADMINISTRATION
PHARMACY BENEFITS MANAGEMENT STRATEGIC HEALTHCARE GROUP,
MEDICAL ADVISORY PANEL, AND
CENTER FOR MEDICATION SAFETY (VA MEDSAFE)

Discontinued Marketing of Tegaserod (Zelnorm®) for Safety Reasons

I. **ISSUE** – On March 30, 2007, Novartis suspended US marketing and sales of tegaserod in compliance with the Food and Drug Administration's (FDA) request which was based on a retrospective analysis of pooled clinical trial data showing increased risk of serious cardiovascular adverse events associated with use of tegaserod compared to placebo.

II. **BACKGROUND** – Novartis reported results of an analysis involving 29 short-term randomized, controlled clinical trials of tegaserod which included over 18,000 patients in the clinical trial database. Serious cardiovascular events (angina, MI, and stroke) occurred in 13 of 11,614 (0.11%) tegaserod-treated patients compared to 1 of 7,031 (0.01%) placebo-treated patients (p=0.024). All patients affected had pre-existing cardiovascular disease.

III. **DISCUSSION** – Tegaserod was approved in July 2002 for the short-term treatment of constipation-predominant irritable bowel syndrome (IBS) in women. Subsequently, the drug was approved in August 2004 for the treatment of chronic constipation in men and women under age 65.

In January 2006, VA PBM provided criteria for nonformulary use of tegaserod based on available evidence reviewed in the PBM Drug Monograph for tegaserod. A preliminary utilization evaluation was conducted by VAMedSAFE to look at variations in prescribing patterns. Although not an approved indication, patients with gastroesophageal reflux disease (GERD) appeared to be the largest users of tegaserod. Prescription database extraction of patients on tegaserod and merging with selected diagnoses codes revealed ~65% of patients with GERD, ~22% with IBS, ~11% with constipation, and ~2% with diabetic gastroparesis (n=1726).

IV. **RECOMMENDATIONS –** As a result of the tegaserod discontinuation, the PBM and VA MedSAFE will conduct an internal review to determine the rate of cardiovascular events in veteran patients who were on tegaserod therapy from the point of its entry into the VA system up to market withdrawal.

In view of the high volume of unlabelled use of tegaserod, in conjunction with the risk of serious cardiovascular adverse events, the VA PBM and VAMedSAFE is issuing this safety bulletin to alert healthcare providers to promptly evaluate patients for discontinuation. Patients receiving tegaserod therapy for GERD should be transitioned to standard GERD therapies. VA PBM and VAMedSAFE realize that many individual medical centers have initiatives in place to address patients currently on tegaserod therapy. To facilitate this effort on a national level, a list of active tegaserod users will be available to assist VISNs with the prompt discontinuation of tegaserod therapy.

VA patient and provider letters may be accessed at the VA PBM Website: http://www.pbm.va.gov

For more information, please refer to the following links:
http://www.fda.gov/cder/drug/advisory/tegaserod.htm
http://www.fda.gov/bbs/topics/NEWS/2007/NEW01597.html