FDA Announces Drug Withdrawals, Recalls and Safety Warnings

Last month, the FDA announced that several drugs have either been removed from the market or were issued safety warnings. FLRx has notified our affected members who were prescribed these medications within the last 120 days and we have provided physicians with patient listings. Claims for pergolide, Zelnorm® and trimethobenzamide suppositories will no longer be processed through our system.

**Pergolide Products (March 29):** Pergolide drug products (Permax®) used to treat Parkinson’s disease, were removed from the market due to a serious risk for heart valve damage. Two studies published in the New England Journal of Medicine in January 2007 demonstrated a link between pergolide and cardiac valve regurgitation. (NEJM 356:29-38. and NEJM 356:39-46.)

For patients currently taking pergolide, the FDA is recommending that prescribers assess the patient’s need for dopamine therapy, and if continued therapy is necessary, substitute an alternative agent. Pergolide should not be stopped abruptly, rather dosing should be gradually decreased. ([http://www.fda.gov/cder/drug/advisory/pergolide.htm](http://www.fda.gov/cder/drug/advisory/pergolide.htm))

**Zelnorm® (March 30):** Novartis Pharmaceuticals Corporation has voluntarily discontinued the marketing of Zelnorm based on the recent findings of an increase in risk of serious cardiovascular adverse events associated with its use. Zelnorm is approved for short-term treatment of women with irritable bowel syndrome with constipation and for patients younger than 65 years with chronic constipation. This action was based on the analysis of 29 short-term, randomized, controlled trials involving over 18,000 patients which showed an increased risk in cardiovascular adverse events (angina, heart attack, stroke, etc.) associated with Zelnorm use when compared to placebo. From this analysis, the FDA has concluded that the benefits from Zelnorm do not outweigh the risks. The absolute difference in cardiovascular events was small, but statistically significant (0.1% in the Zelnorm group and 0.01% in the placebo group).

The FDA recommends that patients taking Zelnorm seek immediate medical attention if they experience severe chest pain, shortness of breath, dizziness, sudden onset of weakness or difficulty walking, or other symptoms of heart attack or stroke. ([http://www.fda.gov/cder/drug/advisory/tegaserod.htm](http://www.fda.gov/cder/drug/advisory/tegaserod.htm))

**Suppository Products Containing Trimethobenzamide (April 6):** The FDA issued a press release stating that as part of its ongoing efforts to review unapproved marketed drugs and the DESI project, manufacturers will no longer be permitted to produce and distribute suppository forms of trimethobenzamide, a medication typically used for the treatment of nausea and vomiting. These products are also sold under the names Tigan®, Tebamide®, T-Gen®, Trimazide®, and Trimethobenz®. The FDA has determined that these products lack evidence of efficacy. This notice does not apply to other FDA-approved dosage forms of trimethobenzamide, such as capsules and injections. All companies currently producing these suppositories will be required to cease shipping by May 9, 2007. ([http://www.fda.gov/bbs/topics/NEWS/2007/NEW01601.html](http://www.fda.gov/bbs/topics/NEWS/2007/NEW01601.html))
**Grifulvin V® Oral Suspension and Griseofulvin V Oral Suspension (April 10):**
Ortho Dermatological, a Division of Ortho-McNeil Pharmaceutical, Inc. manufacturer of Grifulvin V® Oral Suspension and griseofulvin V Oral Suspension (manufactured by Patriot Pharmaceuticals, L.L.C.), voluntarily recalled certain lots of the drugs from the U.S. market. These medications are approved for treatment of ringworm and other fungal infections.

The recall is supported by the FDA and follows two reports of glass fragments found in bottles of the liquid formation only (no other dosage form has been recalled). There have been no reports of adverse events from the reported glass fragments.

The lots which contained the bottles with glass fragments were shipped to distributors in the United States only between August 23, 2005 and March 14, 2007. Lot numbers can be found on the back of the product label only on four-ounce (120 mL) glass bottles filled by the manufacturer. Lot numbers are also posted on the FDA Web site (www.fda.gov) and at www.aboutgrifulvin.com.

Patients in possession of the medication should contact the pharmacy where they purchased the drug to determine if they have the product that has been recalled.

**Combivir® Safety Warning (April 10)**
GlaxoSmithKline (GSK) issued a warning with regard to misbranded bottles of Ziagen tablets labeled as Combivir. This alert was issued after two bottles labeled as Combivir were found to contain Ziagen. The FDA believes that the problem was isolated to one pharmacy in California. However, a letter was issued to all pharmacies encouraging them to check all bottles in stock and notify GSK immediately if they found something other than Combivir in bottles labeled as Combivir.

**Zanaflex® (tizanidine) (April 11)**
Acorda Therapeutics and the FDA informed health care professionals of changes to the “Contraindications and Warnings” sections of the product labeling for Zanaflex, used to treat spasticity. In pharmacokinetic studies where tizanidine was co-administered with either fluvoxamine or ciprofloxacin (CYP1A2 inhibitors), the serum concentration of tizanidine was significantly increased and potentiated its hypotensive and sedative effects.

Although there are no clinical studies evaluating the effects of other CYP1A2 inhibitors on tizanidine, co-administration of tizanidine with other CYP1A2 inhibitors (zileuton, other fluoroquinolones, antiarrythmics, cimetidine, famotidine, oral contraceptives, acyclovir and ticlopidine) should be avoided. http://www.fda.gov/medwatch/safety/2007/safety07.htm#Zanaflex

**Update to FluMist® Article Published in Rx Facts:** The current 2006 CDC guidelines recommend influenza vaccination in children age 6 to 59 months, extending the age range for routine vaccination from previously reported 6-23 months (January 2007 issue of Rx Facts). The current CDC guidelines can be found at http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5510a1.htm

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