



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2015-N-1663]

Determination That Ondansetron (Ondansetron Hydrochloride) Injection, USP in PL 2408 Plastic Container, 32 Milligrams in 50 Milliliters, Was Withdrawn From Sale for Reasons of Safety or Effectiveness

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) has determined that Ondansetron (ondansetron hydrochloride (HCl)) Injection, USP in PL 2408 Plastic Container, 32 milligrams (mg) in 50 milliliters (mL), single intravenous (IV) dose, was withdrawn from sale for reasons of safety or effectiveness. The Agency will not accept or approve abbreviated new drug applications (ANDAs) for Ondansetron (ondansetron HCl) Injection, USP in PL 2408 Plastic Container, 32 mg/50 mL, single IV dose.

FOR FURTHER INFORMATION CONTACT: Emily Helms Williams, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 6280, Silver Spring, MD 20993-0002, 301-796-3381.

SUPPLEMENTARY INFORMATION: In 1984, Congress enacted the Drug Price Competition and Patent Term Restoration Act of 1984 (Pub. L. 98-417) (the 1984 amendments), which authorized the approval of duplicate versions of drug products under an ANDA procedure.

ANDA applicants must, with certain exceptions, show among other things that the drug for which they are seeking approval contains the same active ingredient in the same strength and dosage form as the “listed drug,” which is a version of the drug that was previously approved. ANDA applicants do not have to repeat the extensive clinical testing otherwise necessary to gain approval of a new drug application (NDA).

The 1984 amendments include what is now section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)), which requires FDA to publish a list of all approved drugs. FDA publishes this list as part of the “Approved Drug Products With Therapeutic Equivalence Evaluations,” which is known generally as the “Orange Book.” Under FDA regulations, drugs are removed from the list if the Agency withdraws or suspends approval of the drug’s NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (21 CFR 314.162).

A person may petition the Agency to determine, or the Agency may determine on its own initiative, whether a listed drug was withdrawn from sale for reasons of safety or effectiveness. This determination may be made at any time after the drug has been withdrawn from sale but must be made prior to approving an ANDA that refers to the listed drug (21 CFR 314.161). FDA may not approve an ANDA that does not refer to a listed drug.

Ondansetron (ondansetron HCl) Injection, USP in PL 2408 Plastic Container, 32 mg/50 mL, single IV dose, is the subject of NDA 021915, held by Baxter Healthcare Corporation (Baxter), and initially approved on December 27, 2006. The product is indicated for prevention of nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy in adult patients. It was approved under the pathway described by section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(b)(2)). Baxter’s

application relied in part on FDA's finding of safety and effectiveness for ZOFTRAN, NDA 020007, held by GlaxoSmithKline (GSK).

In September 2011, FDA issued a Drug Safety Communication noting concerns that the 32 mg single IV dose of ZOFTRAN, NDA 020007, and generic versions of that product could increase the risk of abnormal changes in the electrical activity of the heart, which could result in a potentially fatal abnormal heart rhythm. Specifically, the Agency noted that the 32 mg single IV dose of ondansetron could cause QT prolongation, which can lead to a serious and sometimes fatal heart rhythm called Torsades de Pointes. At FDA's request, GSK conducted a study to assess that risk. That study identified a significant QT prolongation effect in connection with the 32 mg single IV dose of Ondansetron. Based on this data, FDA approved GSK's supplemental application to remove the 32 mg single IV dose information from the labeling for ZOFTRAN and has worked with manufacturers of all 32 mg, single IV dose ondansetron products to have them removed from the market.

In a letter dated September 5, 2012, Baxter notified FDA that Ondansetron (ondansetron HCl) Injection, USP in PL 2408 Plastic Container, 32 mg/50 mL, single IV dose, was being discontinued, and FDA moved the drug product to the "Discontinued Drug Product List" section of the Orange Book. In a letter dated November 27, 2012, Baxter requested withdrawal of NDA 021915 for Ondansetron (ondansetron HCl) Injection, USP in PL 2408 Plastic Container, 32 mg/50 mL, single IV dose. In a contemporaneous notice, FDA is announcing that it is withdrawing approval of NDA 021915.

We have carefully reviewed our files for records concerning the withdrawal of Ondansetron (ondansetron HCl) Injection, USP in PL 2408 Plastic Container, 32 mg/50 mL, single IV dose, from sale. We have also evaluated relevant literature and data. FDA has

determined under §§ 314.161 and 314.162(a)(2), that Ondansetron (ondansetron HCl) Injection, USP in PL 2408 Plastic Container, 32 mg/50 mL, single IV dose, was withdrawn from sale for reasons of safety.

Accordingly, the Agency will remove Ondansetron (ondansetron HCl) Injection, USP in PL 2408 Plastic Container, 32 mg/50 mL, single IV dose, from the list of drug products published in the Orange Book. FDA will not accept or approve ANDAs that refer to this drug product.

Dated: June 4, 2015.

Leslie Kux,

Associate Commissioner for Policy.

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