FDA News Release

FDA warns API manufacturer involved in valsartan recall, provides information for patients taking these medications

For Immediate Release

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Release

The U.S. Food and Drug Administration today released a **warning letter (/ICECI/EnforcementActions/WarningLetters/ucm628009.htm)** issued to Zhejiang Huahai Pharmaceutical Co. Ltd. (ZHP), in Linhai, Taizhou Zhejiang China, the manufacturer of the active pharmaceutical ingredient (API) found in valsartan that is the subject of an ongoing FDA investigation into probable cancer-causing impurities in certain commonly prescribed heart medicines. The letter outlines several manufacturing violations at ZHP's Chuannan facility, including impurity control, change control and cross contamination from one manufacturing process line to another. The warning letter is another step forward in the ongoing investigation. The agency is still looking into the root cause of the impurity.

"We're continuing to investigate and take action to protect patient health and safety from products in this angiotensin II receptor blocker class that have been found to have dangerous impurities. As part of that investigation, we've uncovered serious manufacturing violations at ZHP, which is one of the manufacturing facilities that has been linked to these products. The issues cited in the warning letter are associated with the nitrosamine impurities found in these drugs, and these violations reveal a disturbing lack of oversight at this API manufacturer that puts patients at risk," said FDA Commissioner Scott Gottlieb, M.D.

The ZHP facility manufactures API including valsartan, a drug in the angiotensin II receptor blocker (ARB) class used to treat high blood pressure and heart failure. On September 28, the FDA also put this facility on **import alert (https://www.accessdata.fda.gov/cms_ia/importalert_189.html)**, stopping all API made there and finished drug products made using its API from legally entering the U.S. The agency put ZHP on import alert based, in part, on high levels of impurities found in ZHP's API.

The FDA **announced (/NewsEvents/Newsroom/PressAnnouncements/ucm613532.htm)** recalls of valsartan beginning in July due to the presence of N-Nitrosodimethylamine (NDMA) in API supplied by ZHP. Subsequent international investigations expanded to include all manufacturers of API and finished drugs in the ARB class and have resulted in additional recalls of valsartan, irbesartan, and losartan-containing products found to contain NDMA and N-Nitrosodiethylamine (NDEA) – both known animal and suspected human carcinogens.

There may be confusion regarding which products are affected by ARB recalls and which are not, especially concerning the most recent U.S. recalls of valsartan-containing products using API manufactured by Mylan that tested positive for unacceptable levels of NDEA. Certain ARB products have been recalled, and certain products that contain ARBs and one or more other active ingredients in a single dosage form have been recalled. It is important to note that the API in these products besides valsartan, irbesartan or losartan are not necessarily under a recall. As an example, valsartan/amlodipine/hydrochlorothiazide is one product that has been **recalled (/Safety/Recalls/ucm626802.htm)**. Neither amlodipine or hydrochlorothiazide are currently under recall. Similarly, losartan potassium and hydrochlorothiazide 100mg/25mg is a **recalled (/Safety/Recalls/ucm625492.htm)** product. The agency asks the public to pay careful attention to the agency's website for the most accurate and up-to-date information. The agency's website provides lists of **valsartan products under recall (/downloads/Drugs/DrugSafety/UCM615703.pdf)**, **valsartan products not under recall (/downloads/Drugs/DrugSafety/UCM615704.pdf)** and **irbesartan products under recall (/downloads/Drugs/DrugSafety/UCM624627.pdf)** for patients, health care providers and pharmacists to accurately confirm which products are affected.

The FDA continues to test all ARBs for the presence of impurities and has publicly posted two methods for manufacturers and regulatory agencies around the world to test their ARBs for the unexpected NDMA and NDEA impurities.

Patients taking any recalled ARB should continue taking their current medicine until their pharmacist provides a replacement or their doctor provides an alternative treatment option. It also is important to know that not all ARBs contain NDMA or NDEA, so pharmacists may be able to provide a refill of medication not affected by the recall, or doctors may prescribe a different medication that treats the same condition.

Patients, health care providers and pharmacists may contact the FDA's Division of Drug Information for any questions regarding ARB recalls. Visit the FDA's **ARB recall webpage (/Drugs/DrugSafety/ucm613916.htm)**, call 855-543-3784 or email **druginfo@fda.hhs.gov (mailto:druginfo@fda.hhs.gov)** for more information. A **question and answer webpage (/Drugs/DrugSafety/ucm626122.htm)** also provides information on these recalls.

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

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For More Information

- **FDA updates on valsartan recalls (/Drugs/DrugSafety/ucm613916.htm)**
- **Questions and Answers: Impurities found in certain generic angiotensin II receptor blocker (ARB) products (/Drugs/DrugSafety/ucm626122.htm)**
- **Statement from FDA Commissioner Scott Gottlieb, M.D., and Janet Woodcock, M.D., director of the Center for Drug Evaluation and Research, on FDA's ongoing investigation into valsartan impurities and recalls and an update on FDA's current findings (/NewsEvents/Newsroom/PressAnnouncements/ucm619024.htm)**

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