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Update on review of recalled valsartan medicines

Preliminary assessment of possible risk to patients

EMA is conducting a review of the possible health effects in patients who may have taken valsartan medicines containing NDMA[1] – an impurity found in the active substance manufactured by Zhejiang Huahai Pharmaceuticals.

NDMA is classified as a probable human carcinogen (a substance that could cause cancer) based on animal tests. It is present in some foods and water supplies but is not expected to cause harm when ingested in very low levels.

Following a preliminary evaluation, EMA estimates that there could be one extra case of cancer for every 5,000 patients taking the affected medicines at the highest valsartan dose (320 mg) every day for 7 years. This is based on average levels of this impurity detected in the active substance from Zhejiang Huahai Pharmaceuticals (60 parts per million).

The possible cancer risk has been extrapolated from animal studies and should be considered in the context of the lifetime risk of cancer in the EU (1 in 3) and NDMA exposure from other sources.

This preliminary estimate is based on the assumption that the NDMA present in the active substance is carried over in the final product in the same amount.

Companies that had used the active substance from Zhejiang Huahai in their valsartan medicines are required to test samples they hold to determine the actual NDMA levels in the final products. Additional checks are being carried out by EU official control laboratories. Once data from all these tests are available, EMA will be able to provide more information on the risk that the impurity may have posed for patients in the EU.

It is important to note that there is no immediate risk to patients. Patients taking the affected medicines who have not yet switched to an alternative should not stop taking their medicines without consulting their doctor or pharmacist.

Valsartan medicines are used for patients with serious or potentially serious conditions of the circulatory system (high blood pressure, a recent heart attack and heart failure). It is therefore not advisable to go without treatment if a treatment has been prescribed.

All valsartan medicines containing the active substance from Zhejiang Huahai Pharmaceuticals have been recalled from pharmacies in the EU but several other valsartan medicines not affected by the

[1] N-nitrosodimethylamine

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impurity are available. Patients who want more information about their treatments should contact their doctor or pharmacist. Further information is provided by national medicines authorities.

NDMA was an unexpected impurity believed to have formed as a side product after Zhejiang Huahai introduced changes to its manufacturing process in 2012. No other active substances produced by the company are affected.

EMA is working closely with international partners and will provide further information on its website as the review progresses.

More about the medicine

Valsartan is an angiotensin-II-receptor antagonist used to treat hypertension (high blood pressure), recent heart attack and heart failure. It is available on its own or in combination with other active substances.

The review covers all medicines that contain valsartan supplied by Zhejiang Huahai Pharmaceuticals. As a precaution, the review will also consider whether other valsartan medicines may be affected.

More about the procedure

The review of valsartan medicines in relation to NDMA found in the active substance from Zhejiang Huahai Pharmaceuticals was triggered by the European Commission on 5 July 2018 Article 31 of Directive 2001/83/EC.

The review is being carried out by the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which will adopt the Agency's opinion. The CHMP opinion will then be forwarded to the European Commission, which will issue a final legally binding decision applicable in all EU Member States.