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EU inspection finds Zhejiang Huahai site non-compliant for manufacture of valsartan

EMA and national authorities considering impact on other active substances produced at the site

An inspection by EU authorities in collaboration with EDQM has found that Zhejiang Huahai did not comply with Good Manufacturing Practice (GMP) in the manufacture of valsartan at the Chuannan site in Linhai, China.

As a result, a statement of non-compliance for the manufacture of valsartan has been issued and the site is no longer authorised to produce valsartan (and its intermediates) for EU medicines. This means that marketing authorisation holders in the EU are prohibited from using valsartan from the site for the production of medicines.

This action comes after product recalls and the subsequent suspension of the company's CEP[1] for valsartan (a certificate of compliance with European standards for quality testing) in July 2018. This already prohibited the supply of the company's valsartan in the EU due to the presence of an impurity N-nitrosodimethylamine (NDMA).

The latest European inspection, which focused on the manufacture of valsartan and was completed in September 2018, found several weaknesses at Zhejiang Huahai, including deficiencies in the way the company investigated the presence of NDMA and another impurity N-nitrosodiethylamine (NDEA) in its valsartan products.

The non-compliance statement, which applies only to the manufacture of valsartan, is available on the EudraGMP website.

The site has recently also been inspected by the US Food and Drug Administration (FDA), which has issued an import alert stopping all active substances produced by Zhejiang Huahai's Chuannan site and all medicines containing those active substances from entering the United States. FDA has not announced additional product recalls other than those already in place for valsartan medicines, similar to the recalls in the EU.

EMA and national authorities in the EU are now actively considering all available evidence, including the outcomes of the European and US inspections, as part of the ongoing process of evaluating the

[1] CEP: certificate of suitability to the monographs of the European Pharmacopoeia

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

Zhejiang Huahai manufacturing site. This will determine what further EU action may be required for other active substances produced by the site.

The detection of NDMA (a substance that could cause cancer) in valsartan from Zhejiang Huahai led to an EU-wide review of valsartan medicines, which was subsequently extended to other sartans medicines.

This review is still ongoing. EMA will continue working with national authorities, international partners and EDQM and will provide updates as more information becomes available.

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.

More about the procedure

The review of valsartan medicines was triggered by the European Commission on 5 July 2018 under Article 31 of Directive 2001/83/EC. On 20 September 2018, the review was extended to include medicines containing candesartan, irbesartan, losartan and olmesartan.

The review is being carried out by EMA's 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.