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Impure valsartan API prompts recalls in EU

Hundreds of marketing authorisations held by major generics players – including Accord's Actavis, Aurobindo, Gedeon Richter, Sandoz, Sanofi's Zentiva, and Teva – have been affected by recalls across Europe of medicines containing valsartan, prompted by the discovery of an impurity in the active pharmaceutical ingredient (API) supplied by China's Zhejiang Huahai. Health Canada has also issued a recall.

Announcing that it was reviewing medicines containing valsartan supplied by Zhejiang Huahai, the European Medicines Agency (EMA) agency said this was "triggered after the firm detected an impurity, N-nitrosodimethylamine (NDMA), in the valsartan active substance. NDMA was "classified as a probable human carcinogen", the agency noted. "While the review is under way," the EMA confirmed, "national authorities across the European Union (EU) are recalling medicines containing valsartan supplied by Zhejiang Huahai."

"The presence of NDMA was unexpected and is thought to be related to changes in the way the active substance was manufactured," the EMA stated. Noting that its review would be carried out by the agency's committee for human medicinal products (CHMP), the EMA said this would "investigate the levels of NDMA in these valsartan medicines, its possible impact on patients who have been taking them, and what measures can be taken to reduce or eliminate the impurity from future batches produced by the company".

Moreover, the EMA added, the CHMP review would also "consider whether other valsartan medicines may be affected". Patients were advised to keep taking their valsartan medicine unless told otherwise by their doctor or pharmacist, and were advised that they may be given a different valsartan medicine – or alternative treatment – when their next prescription was dispensed. "Further information will be provided once available," the agency stated.

In an earlier version of this story, **Generics *bulletin*** provided false information regarding Krka's valsartan product. Neither Krka's valsartan active substance nor Krka's medicines contain the discovered impurity and are thus not subject to any recalls based on intensive communication with regulatory authorities throughout Europe.

WHO invites bio prequalification

An invitation to participate in a pilot procedure for the prequalification of both branded and biosimilar rituximab and trastuzumab has been published by the World Health Organization (WHO). First announced last year (**Generics *bulletin***, 15 September 2017, page 5) – after the WHO announced that it would start prequalifying the two oncology treatments (**Generics *bulletin***, 12 May 2017, page 13) – the scheme, titled 'pilot procedure for prequalification of biotherapeutic products and similar biotherapeutic products', has been billed by the WHO as "a step forward to support national and global efforts to increase access to and the affordability of biotherapeutic products and their corresponding similar biotherapeutic products".

If products meet WHO standards, they will be included on the WHO list of prequalified products acceptable in principle for procurement by United Nations (UN) agencies and WHO member states. "The WHO's prequalification team has developed a WHO pilot procedure for prequalification of two biotherapeutic products, rituximab or trastuzumab," the WHO outlined, "and is inviting manufacturers to submit an expression of interest for product evaluation to the WHO prequalification team." The formal invitation specifies rituximab for injection in 100mg/10ml and 500mg/50ml presentations, and trastuzumab powder for injection in 60mg, 150mg and 440mg in vial formats. "No fees are applicable for this first invitation under the WHO pilot procedure," the organisation notes.