Control of nitrosamine impurities in sartans: revision of five Ph....

European Pharmacopoeia
Monograph
News
13 June 2019
Strasbourg, France

The European Commission has issued its **final legally binding decision on medicines containing valsartan, candesartan, irbesartan, losartan and olmesartan** on 2 April 2019. This decision was based on the scientific assessment of angiotensin-II-receptor antagonists (sartans) containing a tetrazole group performed by the Committee for Medicinal Products for Human Use (CHMP), the conclusions of which are set out in Annex I to the *European Commission Decision C(2019) 2698 final*.

The five sartans concerned by this Decision are each covered by an individual monograph in the Ph. Eur. Therefore, the monographs have been revised to align the Ph. Eur. requirements to this Decision for the transitional period of 2 years by:

- Adding the following Production section:

  "As *N*-nitrosodimethylamine (NDMA) and *N*-nitrosodiethylamine (NDEA) are classified as probable human carcinogens, manufacturers must ensure that their manufacturing process does not generate such impurities and develop appropriate control strategies. To allow manufacturers to make the necessary changes to their process, a transition period has been agreed by Competent Authorities and strict temporary limits on levels of these impurities introduced in the Test section."

- Revising the Test section and adding the following requirement

  "**Nitrosamines**. Carry out the test by a suitable method. The substance to be examined does not contain either NDMA or NDEA above the limits provided below or both impurities at whatever level:

API	**NDEA** Limit in ppm in API	**NDMA** Limit in ppm in API
Valsartan	0.082	0.300
Losartan	0.177	0.640
Olmesartan	0.663	2.400
Irbesartan	0.088	0.320

Candesartan	0.820	3.000

The Ph. Eur. Commission adopted the revised monographs for publication in the 10 th edition of the Ph. Eur. (publication schedule: July 2019; implementation date: 1 st January 2020). These revised texts were not published in Pharmeuropa for public enquiry as the changes made are in line with the *European Commission Decision C(2019) 2698 final* which is applicable in all EU Member states (and with EEA relevance).