Press release

23 February 2021, Strasbourg, France

Control of *N*-nitrosamine impurities in sartans: revision and rapid implementation of five Ph. Eur. monographs

On 9 July 2020, the EMA's Committee for Medicinal Products for Human Use (CHMP) published its opinion pursuant to Article 5(3) of Regulation (EC) No 726/2004 regarding the detection, management and prevention of the presence of *N*-nitrosamines in medicinal products for human use (see the report published on 25 June 2020). The CHMP subsequently decided to apply these recommendations to "sartans medicinal products" (see the EMA news item published on 13 November 2020).

To ensure that European Pharmacopoeia (Ph. Eur.) requirements are aligned with the latest regulatory decisions, the Ph. Eur. Commission decided to revise the five monographs on sartans containing a tetrazole ring, published in the 10th Edition of the Ph. Eur. (*Valsartan*, *Losartan potassium*, *Irbesartan*, *Candesartan cilexetil* and *Olmesartan medoxomil*) by:

- rewording the "Production" section (the example below is taken from Valsartan) in the monograph as follows:

  As N-nitrosamines are classified as probable human carcinogens, their presence in valsartan should be avoided or limited as much as possible. For this reason, manufacturers of valsartan for human use are expected to perform an assessment of the risk of N-nitrosamine formation and contamination during their manufacturing process; if this assessment identifies a potential risk, the manufacturing process should be modified to minimise contamination and a control strategy implemented to detect and control N-nitrosamine impurities in valsartan. General chapter 2.5.42. N-Nitrosamines in active substances is available to assist manufacturers.

- deleting the *N*-nitrosamines test section.

The Ph. Eur. Commission adopted the revised monographs using the "rapid revision" procedure, with an implementation date of 1 April 2021 (see *Guide for the work of the European Pharmacopoeia*, §6.3). The PDF versions of the texts are now available on the EDQM website (here). The revised monographs will be added to the online and downloadable versions of the Ph. Eur. as of Supplement 10.4. They will be included in the printed version from Supplement 10.6.

These revised texts were not published in Pharmeuropa for public enquiry as the changes made reflect the latest EMA recommendations.

At the same session, the Ph. Eur. Commission also decided to revise two general monographs, *2034 Substances for pharmaceutical use* and *2619 Pharmaceutical preparations,* to include recommendations for manufacturers to evaluate and address the risk of presence of *N*-nitrosamine impurities in active substances for human use and medicinal products for human use. These two general monographs will be published in Pharmeuropa 33.2 (April-June 2021): don't miss this opportunity!

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Note for the Editor: Further information is available on the internet site **https://www.edqm.eu/**.

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The EDQM is a leading organisation that protects public health by enabling the development, supporting the implementation and monitoring the application of quality standards for safe medicines and their safe use. Our standards are recognised as a scientific benchmark worldwide. The European Pharmacopoeia is legally binding in member states.[1] The EDQM also develops guidance and standards in the areas of blood transfusion, organ transplantation and consumer health issues.

1. There are 40 members of the European Pharmacopoeia Commission: *Austria, Albania, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Republic of Moldova, Montenegro, Netherlands, North Macedonia, Norway, Poland, Portugal, Romania, Serbia, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, Turkey, Ukraine, United Kingdom and the European Union.*

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