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Update on nitrosamine impurities: EMA continues to work to prevent impurities in medicines

Following an EU safety review, which concluded on strict legally binding limits for nitrosamine impurities in sartan blood pressure medicines, EMA continues to work to ensure manufacturers are taking appropriate measures to avoid or keep impurities below acceptable limits.

Based on experience from the review of sartans, EMA is launching an exercise with experts from across the EU regulatory network including national authorities, the European Directorate for the Quality of Medicines & HealthCare (EDQM) and the European Commission to consider how to prevent such incidents in future and to see if their management can be improved, should they occur.

EMA will publish the outcome of the exercise in due course, including information on any further actions that may be required.

As part of strengthened monitoring of manufacturing, EMA and national authorities are also requesting as precaution that companies using certain reagents to manufacture the diabetes medicine pioglitazone test their products and check their processes to rule out the presence of nitrosamine impurities, in particular nitrosodimethylamine (NDMA).

The request follows the detection of low levels of NDMA in a few batches of pioglitazone manufactured by Hetero Labs in India, which were within strict limits previously set for sartans and are considered acceptably safe.

Nitrosamines are classified as probable human carcinogens (i.e. substances that could cause cancer). They are present in foods and water, and most people are exposed to them daily in small amounts. However, their presence in medicines is largely avoidable and the relatively low risk they pose to patients does not make them acceptable.

Nitrosamines were first detected in sartan medicines in June 2018. Authorities in the EU took swift action: affected batches were recalled from pharmacies; patients and healthcare professionals were given appropriate advice on alternative treatments; and medicines across the EU were subjected to additional tests to guarantee they did not pose unacceptable risks to patients.

EMA will continue working closely with national authorities and international partners to ensure that manufacturers are taking appropriate measures with respect to nitrosamines.

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