



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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EMA finalises opinion on presence of nitrosamines in medicines

EMA's human medicines committee (CHMP) has issued an opinion requiring companies to take measures to limit the presence of nitrosamines in human medicines as far as possible and to ensure levels of these impurities do not exceed set limits.

The measures will ensure that nitrosamines are either not present or are present below levels identified to protect public health.

Companies will be required to have appropriate control strategies to prevent or limit the presence of these impurities and, where necessary, improve their manufacturing processes.

Companies will also have to evaluate the risk of nitrosamines being present in medicines and carry out appropriate tests if a risk is identified.

Nitrosamines are classified as probable human carcinogens (substances that could cause cancer). The limits for nitrosamines in medicines have been set using internationally agreed standards (ICH M7(R1)) based on lifetime exposure. Patients should generally not be exposed to a lifetime risk of cancer exceeding 1 in 100,000 from nitrosamines in their medicines.

Detailed information for companies, including timelines, will soon be available in updated documents on [EMA's nitrosamines webpage](#). In the meantime, companies should continue to follow current instructions.

EU regulators first became aware of nitrosamines in medicines in mid-2018 and took regulatory actions, including recalling medicines and stopping the use of active substances from certain manufacturers. A subsequent CHMP review of sartan blood pressure medicines in 2019 led to [new requirements](#) for the manufacture of sartans, while its review of ranitidine recommended in 2020 an [EU-wide suspension](#) of ranitidine medicines.

In addition, a recently concluded exercise to draw lessons from the presence of nitrosamines in sartans has made a number of [recommendations](#) to help prevent the presence of impurities in medicines. The recommendations complement the latest requirements from CHMP.

In drawing up the requirements, EMA worked closely with national authorities, the [European Directorate for the Quality of Medicines & HealthCare](#) and international partner agencies. Authorities in the EU, including the European Commission, will work together to ensure that the same measures are taken for medicines irrespective of how they were authorised.

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Authorities in the EU will continue to take all necessary measures to protect patients and reassure them about the quality of their medicines.

Notes

- The opinion from the CHMP follows a request by EMA's Executive Director in accordance with a procedure outlined in [Article 5\(3\) of Regulation \(EC\) No 726/2004](#) by which the CHMP draws up opinions on scientific matters concerning the evaluation of medicinal products for human use.
- The advice from the CHMP draws on work carried out in conjunction with the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), a medicines regulatory body representing the EU Member States, Iceland, Liechtenstein and Norway.
- Detailed information for companies, including timelines, will soon be available in updated documents on [EMA's nitrosamines webpage](#).