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EMA confirms recommendation to suspend all ranitidine medicines in the EU

On 17 September 2020, EMA's human medicines committee (CHMP) confirmed its recommendation to suspend all ranitidine medicines in the EU due to the presence of low levels of an impurity called N-nitrosodimethylamine (NDMA). This follows a re-examination of CHMP's April 2020 opinion, which was requested by one of the companies marketing ranitidine medicines.

NDMA is classified as a probable human carcinogen (a substance that could cause cancer) based on animal studies. It is present in some foods and water supplies and is not expected to cause harm when ingested at very low levels.

Available safety data do not show that ranitidine increases the risk of cancer, and any possible risk is likely to be very low. However, NDMA has been found in several ranitidine medicines above levels considered acceptable, and there are unresolved questions about the source of this impurity.

There is some evidence that NDMA may form from the degradation of ranitidine itself with increasing levels seen over its shelf life. It is not clear if NDMA can also be formed from ranitidine inside the body. Some studies suggest that it can, while others do not. Given the uncertainties, the CHMP has recommended in April 2020 a precautionary suspension of these medicines in the EU.

Ranitidine medicines are used for reducing stomach acid in patients with conditions such as heartburn and stomach ulcers. Alternatives are available and patients should contact their healthcare professionals for advice about which medicine to take.

Following the re-examination, the CHMP maintained the conditions for lifting the suspension of the medicines, including requirements for companies to provide more data on the possible formation of NDMA from ranitidine inside the body. The formation of NDMA in the body is expected to be very low following a single low dose of ranitidine given by injection or infusion (drip). Therefore, the CHMP slightly amended the conditions for lifting the suspension for those ranitidine medicines that are given by injection or infusion as a single, low dose.

Many ranitidine medicines have not been available in the EU for several months. This is because national authorities have recalled them as a precaution while the EMA review was ongoing.

Since 2018 NDMA and similar compounds known as nitrosamines have been detected in several medicines. EU regulators have acted to identify possible sources of the impurities and set strict requirements for manufacturers.

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EMA is continuing to work with national authorities, EDQM,[1] the European Commission and international partners to make sure effective measures are taken to prevent the presence of these impurities in medicines.

Information for patients

- Ranitidine medicines are suspended in the EU as a precaution because of the presence at low levels of an impurity called NDMA.
- Alternative medicines are available to reduce stomach acid. If you have been prescribed ranitidine, your doctor will advise you on an alternative.
- Contact your doctor or pharmacist if you have any questions about which alternative to take.

Information for healthcare professionals

- Ranitidine medicines are suspended in the EU due to the presence of NDMA impurities.
- Available clinical and epidemiological data do not show that ranitidine increases the risk of cancer. However, NDMA has been found in several ranitidine medicines above levels considered acceptable.
- Although the exact source of the impurity in ranitidine is yet to be determined, it is possible that NDMA forms from the degradation of ranitidine even under normal storage conditions. Some studies indicated that ranitidine may cause endogenous NDMA formation by degradation or metabolism in the gastro-intestinal tract, but other studies did not.
- While ranitidine medicines are unavailable, patients should be advised on alternative medicines.
- Healthcare professionals should advise patients who have been taking ranitidine, with or without a prescription, on how to treat or manage conditions such as heartburn and gastric ulcers.

More about the medicine

Ranitidine belongs to a class of medicines known as H2 (histamine-2) blockers, which work by blocking histamine receptors in the stomach and reducing the production of stomach acid.

It is used to treat and prevent conditions such as heartburn and stomach ulcers. Ranitidine-containing medicines have been authorised at national level for about 30 years and are available as tablets, syrups and injectable formulations.

More about the procedure

The review of ranitidine was initiated on 12 September 2019 at the request of the European Commission, under Article 31 of Directive 2001/83/EC.

The review was carried out by the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which adopted its initial opinion in April 2020. Following a re-examination of the opinion, requested by one of the companies concerned, the CHMP made amendments to its recommendation. The final CHMP opinion was forwarded to the

[1] The European Directorate for the Quality of Medicines & HealthCare

European Commission, which issued a final legally binding decision applicable in all EU Member States on 24 November 2020.