20 March 2019
EMA/191666/2019

EMA recommends aligning doses of metamizole medicines and their use during pregnancy and breastfeeding

On 13 December 2018, following a review of medicines containing the painkiller metamizole, EMA recommended that the maximum daily dose of the medicine and the contraindications to its use in pregnancy or women who are breastfeeding should be harmonised for all products on the EU market. The recommendation addressed inconsistencies in the product information for metamizole medicines, which are marketed in many EU member states to treat severe pain and fever that cannot be controlled with other treatments.

The review was carried out by EMA's human medicines committee (CHMP) at the request of Poland, which was concerned by the substantial differences in the recommendations on the use of metamizole in different EU countries, given that it is known the medicine may occasionally cause severe side effects, such as effects on the blood.

The Agency reviewed the available information on the way the medicine is distributed in the body, how it works and the limited data on its effects on the unborn child or breast-fed infant.

EMA's recommendations include setting a maximum single dose by mouth of 1,000 mg, taken up to 4 times daily (a maximum daily dose of 4,000 mg), in patients from 15 years of age. Treatment should start at the lowest recommended dose and only be increased if needed. If given by injection the total daily dose should not exceed 5,000 mg. Doses in younger patients should be based on their body weight but some products may be unsuitable because of their strength.

Although metamizole has been on the market for nearly a century, evidence of its effects in pregnancy and breastfeeding is scarce. The review found little to suggest problems in early pregnancy, and single doses in the first 6 months might be acceptable if other analgesics cannot be used. However, there was some evidence of effects on the kidneys and circulation of the fetus if the medicine were used in the last 3 months of pregnancy, and the medicine should therefore not be used in this period. As a precaution, metamizole should not be used during breastfeeding because the infant may receive high amounts of the medicine in the milk relative to the infant's weight.

EMA's recommendations were forwarded to the European Commission, which issued a final legally binding decision valid across the EU on 20 March 2019.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

Information for patients and healthcare professionals

- EMA has completed a review of the painkiller metamizole, used in many EU countries to treat severe pain and fever that cannot be controlled with other treatments.
- EMA has recommended changes to the product information of metamizole, to ensure that advice on the maximum daily doses and warnings not to use the medicine during the last 3 months of pregnancy or during breastfeeding are consistent across the EU. A summary of the recommended changes will be published on the EMA website.
- Updated summaries of product characteristics (information for healthcare professionals) and package leaflets for patients which contain the new recommendations will be available nationally following the final legal decision issued by the European Commission.
- Patients who have any concerns about their medication should consult their doctor or pharmacist.

More about the medicine

Metamizole (also known as dipyrone) is an analgesic medicine (painkiller) that can also relieve fever and muscle spasm. It has been used for many decades in the EU by mouth, as suppositories or by injection, to treat severe pain and fever that cannot be controlled with other treatments.

Metamizole-containing medicines are available in Austria, Belgium, Bulgaria, Croatia, Czech Republic, Finland, Germany, Hungary, Italy, Latvia, Lithuania, Luxembourg, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia and Spain. They are marketed under a variety of names including Algifen, Algifen Neo, Algi-Mabo, Algoblock, Algocalmin, Algopyrin, Algozone, Alindor, Alkagin, Alvotor, Amizolmet, Analgin, Benalgin, Benlek, Berlosin, Buscapina Compositum, Dialgin, Dolocalma, Flamborin, Freshalgin, Gardan, Generalgin, Hexalgin, Litalgin, Locamin, Metagelan, Metalgial, Metamilan, Metamistad, Metapyrin, Metarapid, Nevralgin, Nodoryl, Nolotil, Novalgin, Novalgina, Novalgine, Novaminsulfon, Novocalmin, Panalgorin, Parakofdal, Piafen, Piralgin, Proalgin, Pyralgin, Pyralgina, Quarelin, Scopolan Compositum, Spasmalgon, Spasmoblok, Tempalgin and Tempimet.

More about the procedure

The review of metamizole was initiated on 31 May 2018 at the request of Poland, under Article 31 of Directive 2001/83/EC.

The review has been carried out by the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which has adopted the Agency's opinion. The CHMP opinion was forwarded to the European Commission, which issued a final legally binding decision applicable in all EU Member States on 20 March 2019.