



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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New recommendations to manage risk of allergic reactions with intravenous iron-containing medicines

On 27 June 2013 the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) completed its review of intravenous iron-containing medicines used to treat iron deficiency and anaemia (low red blood cell counts) associated with low iron levels. The CHMP concluded that the benefits of these medicines are greater than their risks, provided that adequate measures are taken to minimise the risk of allergic reactions.

Intravenous iron medicines are used when iron supplements given by mouth cannot be used or do not work. All intravenous iron medicines have a small risk of causing allergic reactions which can be life-threatening if not treated promptly. The Committee therefore concluded that measures should be put in place to ensure the early detection and effective management of allergic reactions that may occur. Iron preparations should only be given in an environment where resuscitation facilities are available, so that patients who develop an allergic reaction can be treated immediately. In addition, the CHMP considered that the current practice of first giving the patient a small test dose is not a reliable way to predict how the patient will respond when the full dose is given. A test dose is therefore no longer recommended but instead caution is warranted with every dose of intravenous iron that is given, even if previous administrations have been well tolerated.

The CHMP also considered that, during pregnancy, allergic reactions are of particular concern as they can put both the mother and unborn child at risk. Intravenous iron medicines should therefore not be used during pregnancy unless clearly necessary. Treatment should be confined to the second or third trimester, provided the benefits of treatment clearly outweigh the risks to the unborn baby. The Committee also recommended further activities, including yearly reviews of allergic reaction reports and a study to confirm the safety of intravenous iron medicines.

The review of intravenous iron medicines was triggered by the French medicines agency, the National Agency for the Safety of Medicine and Health Products (ANSM), following a national review in 2010. The review highlighted the risk of serious allergic reactions, especially in pregnant women who had received intravenous iron medicines. The CHMP recommendation was sent to the European Commission, which on 13 September 2013 endorsed it and adopted a final decision that is legally binding throughout the EU.



Information to patients

- Intravenous iron medicines are a valuable alternative when iron supplements cannot be given by mouth or have not worked. In rare cases these injections can cause allergic reactions which can be serious. If you are receiving intravenous iron medicines your doctor will closely observe you for any allergic reactions during and for at least 30 minutes after the injection.
- If you are prescribed intravenous iron, you should immediately tell your doctor if you have previously had an allergic reaction to intravenous iron preparations. You should also tell your doctor if you have certain conditions affecting the immune system and involving inflammation (such as rheumatoid arthritis), a history of asthma, eczema or other allergies, as this may make an allergic reaction to intravenous iron preparations more likely.
- If you have signs of an allergic reaction (such as feeling dizzy, swelling of your face and difficulty breathing), you should tell your doctor or nurse straight away.
- If you have any questions you should speak to your doctor or pharmacist.

Information to healthcare professionals

- All intravenous iron preparations can cause serious hypersensitivity reactions which can be fatal.
- As there are data indicating that allergic reactions may still occur in patients who have not reacted to a test dose, a test dose is no longer recommended. Instead caution is warranted with every dose of intravenous iron that is given, even if previous administrations have been well tolerated.
- Intravenous iron medicines should only be administered when staff trained to evaluate and manage anaphylactic and anaphylactoid reactions are immediately available as well as resuscitation facilities. Patients should be closely observed for signs and symptoms of hypersensitivity reactions during and for at least 30 minutes following each injection of an intravenous iron medicine.
- In case of hypersensitivity reactions, healthcare professionals should immediately stop the iron administration and consider appropriate treatment for the hypersensitivity reaction.
- Intravenous iron-containing products are contraindicated in patients with hypersensitivity to the active substance or excipients. Intravenous iron-containing products must also not be used in patients with serious hypersensitivity to other parenteral iron products.
- The risk of hypersensitivity is increased in patients with known allergies or immune or inflammatory conditions and in patients with a history of severe asthma, eczema or other atopic allergy.
- Intravenous iron products should not be used during pregnancy unless clearly necessary. Treatment should be confined to the second or third trimester, provided the benefits of treatment clearly outweigh the potential serious risks to the foetus such as anoxia and foetal distress.
- All prescribers should inform patients of the risk and seriousness of a hypersensitivity reaction and the importance of seeking medical attention if a reaction occurs.

The Agency's recommendations are based on a review of all available data on the risk of hypersensitivity as well as the benefits of intravenous iron medicines:

- Data on the risk of hypersensitivity comes mainly from post-marketing spontaneous reports and the total number of life-threatening and fatal events reported is low. Although the data show a

clear association of intravenous iron medicines and hypersensitivity reactions, the data cannot be used to detect any differences in the safety profile of the different iron medicines.

- In view of the limitations of the data the Committee recommended further activities, including yearly reviews of allergic reaction reports and a study to confirm the safety of intravenous iron medicines.

More about the medicine

Intravenous iron preparations are prescribed when iron supplements given by mouth cannot be used or do not work, especially in patients receiving dialysis for kidney failure, before and after operations, or in case of absorption disorders affecting the gut. The various iron preparations contain complexes of iron bound to other molecules such as sugar molecules. The complexes involved in this procedure were ferric carboxymaltose, iron dextran, sodium ferric gluconate, iron isomaltoside and iron sucrose, which are authorised in all EU Member States via national procedures.

More about the procedure

The review of intravenous iron-containing medicines was initiated at the request of France, under Article 31 of Directive 2001/83/EC. The French medicines agency asked the CHMP to carry out a full assessment of the benefit-risk balance and to issue an opinion on whether the marketing authorisations for these medicines should be maintained, varied, suspended or withdrawn across the European Union.

The CHMP opinion was forwarded to the European Commission, which on 13 September 2013 endorsed it and adopted a final decision that is legally binding throughout the EU.

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