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

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Information on Medicinal Product

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 that were reviewed are iron carboxymaltose, iron dextran, iron gluconate, iron isomaltoside, iron saccharose and iron sucrose, which are authorised in all EU Member States. Ferrologic 20mg/ml solution and Ferinject 50mg/ml are authorised in Malta via national procedures.

ATC code	**Active substances**	**Trade Name**	**Authorisation Number**
B03AC02 Anti-Anemic Preparations	Iron 20mg/ml (as iron sucrose) (100mg/5ml ampoule)	Ferrologic 20mg/ml solution for injection/concentrate for solution for infusion	MA610/00101
B03AC01 Anti-Anemic Preparations	Iron 50mg/ml (as ferric carboxymaltose) (100mg/2ml vial) (500mg/10ml vial)	Ferinject 50mg iron/ml solution for injection/infusion	MA869/00101

Information from European Medicines Agency about the safety concern

The European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) has 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.

The Committee 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

Medicines Authority
203 Level 3, Rue D'Argens, Gzira, GZR 1368 – Malta.
Tel. (+356) 23439000 Fax. (+356) 23439161 www.medicinesauthority.gov.mt

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 will now be sent to the European Commission for the adoption of a legally binding decision throughout the EU.

In Malta

For Healthcare Professionals

- All intravenous iron preparations can cause serious hypersensitivity reactions which can be fatal.
- 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.

Further information

- 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

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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.

Advice for 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.

For more information please visit the European Medicines Agency at **www.ema.europa.eu**

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on I.V. iron medicinal products. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority yellow card scheme or online at **http://www.medicinesauthority.gov.mt/adrportal** or to the marketing authorisation holder or their local representatives.

Dr John J Borg PhD (Bristol)

Post-licensing director

Healthcare professionals and patients are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.

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