Vifor Pharma

December 2013

Strengthened recommendations regarding the risk of serious hypersensitivity reactions with intravenous iron products (Ferinject® solution for injection or infusion)

Dear healthcare professional,

Important information regarding intravenous (IV) iron products has arisen from a European review of their benefits versus risks following concerns about the risk of serious hypersensitivity reactions.

Summary

All IV iron products can cause serious hypersensitivity reactions which can be fatal. These may occur even when a previous administration has been tolerated (including a negative test dose, see below). The benefits of all IV iron products continue to outweigh the risks based on the current available data provided that the following recommendations are followed:

- **IV iron products should not be used in patients with hypersensitivity to the active substance, the product itself, or any of its excipients; and in patients with serious hypersensitivity to other parenteral iron products.**
- **The risk of hypersensitivity is increased in patients with known allergies (including drug allergies) and in patients with immune or inflammatory conditions (e.g. systemic lupus erythematosus, rheumatoid arthritis) as well as in patients with a history of severe asthma, eczema or other atopic allergy. In these patients, IV iron products should only be used if the benefit is clearly judged to outweigh the potential risk.**
- **To minimise risks, IV iron products should be administered in accordance with the posology and method of administration described in the product information for each individual product.**
- **IV iron products should only be administered when staff trained to evaluate and manage anaphylactic/anaphylactoid reactions as well as resuscitation facilities are immediately available.**
- **All prescribers should inform patients of the risk of hypersensitivity before each administration. Patients should be informed of the relevant symptoms and asked to seek urgent medical attention if a reaction occurs.**
- **Patients should be closely monitored for signs of hypersensitivity during and for at least 30 minutes after <u>each</u> administration of an IV iron product.**
- **IV iron products should not be used during pregnancy unless clearly necessary. Treatment should be confined to 2nd or 3rd trimester, if the benefit is clearly judged to outweigh the potential risks for both the mother and the foetus. The risks to the foetus can be serious and include foetal anoxia and distress.**

This letter is sent in agreement with the European Medicines Agency and the Medicines Authority.

Further information

IV iron products are indicated in iron-deficiency situations when the oral route is insufficient or poorly tolerated. The diagnosis must be based on appropriate laboratory tests.

The safety concern

A European review was initiated due to safety concerns regarding the risk of serious hypersensitivity reactions, including when used during pregnancy. All IV iron products can cause serious hypersensitivity reactions, **these may occur even when a previous administration has been tolerated (including a negative test dose). Fatal outcomes have been observed.**

Product information about the risk of hypersensitivity reactions has been reviewed and strengthened, and is now consistent for all IV iron products. Changes to the SmPC specific to hypersensitivity reactions are highlighted in Annex II to this letter. These measures are intended to heighten awareness of the risk of serious hypersensitivity reactions with IV iron products, minimise this risk where possible and to ensure that patients are appropriately informed.

Please note that prescribing and safety information differs between IV iron products and individual summaries of product characteristics (SmPC) should be consulted before and during use as appropriate.

Precautions for use in pregnancy

There are no adequate and well-controlled trials in pregnant women. Studies in animals have shown reproductive toxicity.

Iron-deficiency anaemia occurring in the first trimester of pregnancy can usually be treated with oral iron (intravenous iron should not be used). The benefits of using IV iron products should be carefully weighed against the risks later in pregnancy. Anaphylactic/anaphylactoid reactions occurring with IV iron products may have consequences for both the mother and the foetus (e.g. foetal anoxia, distress, death).

The test dose

Previously a test dose has been recommended for some IV iron products. However, no accurate data are available to clearly support a protective effect of a test dose. The test dose may lead to false reassurance as allergic reactions may occur even in patients that had a negative test dose. **Consequently test doses are no longer recommended and are replaced with the risk minimisation recommendations above.** Caution is warranted with every dose of IV iron product that is given, even if previous administrations have been well tolerated. IV iron products should be administered in accordance with the product specific posology and method of administration described in the product information for each individual product. In case of a hypersensitivity reaction, healthcare professionals are advised to immediately discontinue treatment and consider appropriate medical therapy.

For more details see relevant attached sections of the SmPC (Annex I).

Call for reporting

Any suspected adverse events should be reported to the National Spontaneous Reporting System according to the National Regulation.

ADR Reporting
The Medicines Authority
Post-Licensing Directorate
203 Level 3, Rue D'Argens
GŻR-1368 Gżira
Website: www.medicinesauthority.gov.mt
e-mail: postlicensing.medicinesauthority@gov.mt

Company contact point

Please review carefully the revised enclosed product information and contact Vifor Pharma's authorised representative if you have any additional questions.

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Yours sincerely,

Signature

(*Local Authorised Person)*