PHARMACOSMOS
Committed to Quality

Pharmacosmos UK Ltd
Chiltern House
Howland Road
Thame
OX9 3GQ
United Kingdom

Vifor Pharma
Vifor Pharma UK Limited
The Old Stables
Bagshot Park
Bagshot
GU19 5PJ
United Kingdom

06 November 2013

Strengthened recommendations regarding the risk of serious hypersensitivity reactions with intravenous iron products

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 Irish Medicines Board.

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 product information specific to hypersensitivity reactions are highlighted in the annex of 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 an initial test dose has been recommended for some IV iron products before administration of the first dose to a new patient. 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 an initial test dose before administering the first dose of an IV iron product to a new patient is no longer recommended and is replaced with the risk minimisation recommendations outlined in this letter.** 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. Please note that the advice for administration of a product remains otherwise unchanged.

For more details of the updated information to be included in the product information for all of the IV Iron products see relevant attached sections of the SmPC.

Call for reporting

Please report suspected adverse reactions with any medicine or vaccine to the Irish Medicines Board through the Safety and Quality section online at www.imb.ie, or by contacting;

Pharmacovigilance Section
Irish Medicines Board
Kevin O'Malley House
Earlsfort Centre
Earlsfort Terrace
IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.imb.ie
e-mail: imbpharmacovigilance@imb.ie

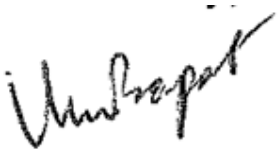
When reporting please ensure to include the name of the specific product administered.

Company contact point

Should you have any questions regarding the use of Cosmofer or Monover , please contact Pharmacosmos UK Ltd Medical Information + 44 (0)1844 269 007 or via email at info@pharmacosmos.co.uk

Should you have any questions regarding the use of Ferinject or Venofer, please contact Vifor Pharma UK Ltd Medical Information + 44 (0)1276853633 or via email at medicalinfo_uk@viforpharma.com

Yours sincerely,



Dr Urmi Bapat
Head of Medical Affairs
PHARMACOSMOS

Dr B R Jackson
Medical Director
Vifor Pharma UK Ltd