Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

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Dear Dr Rylance

Re: IV iron preparations and severe allergic reactions/anaphylaxis

Thank you for your recent inquiry asking about the IV iron preparation and severe allergic reactions/anaphylaxis.

In your email dated 13 July, you mention that a few episodes of severe allergic reactions/anaphylaxis in association with Monofer have been reported to you. If not already done then, I would like to take this opportunity to strongly encourage the healthcare professionals involved or the patients who experienced the events to submit the reports to us through the Yellow Card Scheme website: www.mhra.gov.uk/yellowcard. If the reporters choose to register, they can also keep track of any Yellow Cards that that they send.

Your question is asking for our overall view about the safety of the various IV iron preparations. You will be aware that warnings about the known risk of rare serious hypersensitivity reactions have been present in the product information for all IV Iron products for some time, including that administration should be in a setting where there are staff trained to evaluate and manage anaphylactic/anaphylactoid reactions available and/or where treatment for serious allergic reactions and facilities with the established cardiopulmonary resuscitation procedures are available.

In June 2013, the European Medicines Agency's Committee for Medicines Products for Medicinal Products for Human Use (CHMP) completed its review of intravenous iron-containing medicines used to treat iron deficiency and anaemia associated with low iron level. This review was triggered by the French medicines agency following a national review in 2010 that raised concerns about the risk of serious hypersensitivity reactions, especially in pregnant women.

The IV iron products involved in this European review were Iron carboxymaltose, Iron dextran, Iron isomaltoside, Iron gluconate, Iron isomaltose, Iron saccharose and Iron sucrose.

The review considered all available data from pre-clinical, clinical studies, published literature, post-marketing experience on safety of intravenous iron containing medicinal products in relation to hypersensitivity reactions.

The data reviewed by CHMP showed a clear association of all IV iron medicines and serious hypersensitivity reactions, a particular concern in pregnant women. Based on the available information the CHMP concluded that the benefits of these medicines are greater than their risks provided that adequate measures are taken to manage and minimise the risk of hypersensitivity reactions. These measures relate to the prescribing, administration and monitoring and include the following recommendations:

- a test dose is no longer recommended – caution is necessary with every dose
- strengthened advice on the administration of IV iron products that is to restrict use to an environment where staff trained to evaluate and manage serious hypersensitivity reactions are required to be present and resuscitation facilities are immediately available
- contraindicated in patients with hypersensitivity to the actives or excipients or other parenteral iron products
- should not be used during pregnancy unless clearly necessary. If judged to be necessary by the prescriber then treatment should be restricted to the 2nd or 3rd trimesters

Further details on the European review including the assessment report are available on the European Medicines Agency website and can be accessed via the link: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/referrals/Intravenous_iron-containing_medicinal_products/human_referral_000343.jsp&mid=WC0b01ac05805c516f

In the August 2013 edition of our Drug Safety Update bulletin we published an article on IV irons and serious hypersensitivity reactions and the strengthened recommendations. The full article is available on our website at: https://www.gov.uk/drug-safety-update/intravenous-iron-and-serious-hypersensitivity-reactions-strengthened-recommendations

Data on the risk of hypersensitivity with IV Iron products considered in the European review 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 IV iron products and hypersensitivity reactions, the data cannot be used to detect any difference in the safety profile of the different iron products.

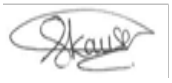
In view of the limitations of the data available at the time of the review, further activities are being undertaken by the marketing authorisation holders including yearly reviews of hypersensitivity reports with the different IV iron products and there's a requirement by the companies to do a study.

The MHRA and its EU partners continue to monitor the incidence of hypersensitivity reactions in association with IV iron products, but there have been no grounds since the completion of the review in 2013 to justify any form of further regulatory intervention in the EU in relation to this known risk.

You also requested for a relevant contact point for medicines safety issues, the first point of contact is the pharmacovigilance service mailbox: Pharmacovigilanceservice@mhra.gsi.gov.uk

I hope this addresses your query.

Yours Sincerely



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