Summary of Risk Management Plan for MonoFer

Part VI – Summary of Activities in the Risk Management Plan by Product

Part VI.2. Elements for a Public Summary

Active substance(s) (INN or common name):	Iron(III) isomaltoside 1000
Pharmaco-therapeutic group (ATC Code):	B03AC
Name of Marketing Authorisation Holder or Applicant:	Pierre Fabre Pharma AG Hegenheimermattweg 183 4123 Allschwil Switzerland
Product(s) concerned (brand name(s)):	MonoFer®

1. Disclaimer

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them.

The RMP summary of MonoFer® is a concise document and does not claim to be exhaustive. As the RMP is an international document, the summary might differ from the “Arzneimittelinformation / Information sur le médicament” approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization.

Please note that the reference document which is valid and relevant for the effective and safe use of MonoFer® in Switzerland is the “Arzneimittelinformation / Information sur le médicament” (see www.swissmedic.ch) approved and authorized by Swissmedic. Pierre Fabre Pharma AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of MonoFer®.

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VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

In 2010, iron deficiency anaemia was considered to be among the most important contributing factors to the global burden of disease affecting both developing and developed countries. Although prevalence varied substantially across communities, iron deficiency anaemia affected 14.9% of the world's population, all ages combined [i][1].

VI.2.2 Summary of treatment benefits

Intravenous iron therapy is beneficial when there is inadequate iron absorption, continued blood loss, noncompliance or intolerance to oral iron therapy. Intravenous (IV) iron preparations are also recommended to treat iron deficiency anaemia as an adjunctive therapy in conjunction with erythropoiesis stimulating agents in chronic kidney disease patients.

VI.2.3 Unknowns relating to treatment benefits

In addition to iron replacement therapy, it is important to treat the underlying cause of the iron deficiency anaemia. Since the aetiology of iron deficiency anaemia is multifactorial, there are a multitude of ways in which this may be carried out, for instance it may involve cessation of anaemia-inducing drugs such as nonsteroidal anti-inflammatory drugs, hormonal treatment for menorrhagia or treatment of irritable bowel disease.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Hypersensitivity	All intravenous iron preparations may cause hypersensitivity reactions varying from mild rashes and flushing to serious and potentially fatal reactions. These reactions have also been reported after previously uneventful doses of intravenous iron. The risk is increased in patients with: • known allergies including drug allergies • a history of severe asthma, eczema or other atopic allergies or • immune or inflammatory conditions (e.g. rheumatoid arthritis, lupus erythematosus)	You must not receive IV iron: • if you are allergic (hypersensitive) to the product or any of the other ingredients of this medicine. • if you have experienced serious allergic (hypersensitive) reactions to other injectable iron preparations. • if you have anaemia not caused by iron deficiency • if you have too much iron (overload) or a problem in the way your body uses iron • if you have liver problems such as 'cirrhosis' or 'hepatitis' Administration is provided by staff trained to evaluate and manage hypersensitivity reactions and patients are monitoring for early symptoms. Early symptoms usually resolve or improve upon treatment with antihistamine and steroid products. In more severe cases, treatment with adrenaline may be required. If hypersensitivity reactions or signs of intolerance occur during administration, the treatment must be stopped immediately.

Important potential risks

Risk	What is known	Preventability
Haemosiderosis	Based on currently available data in the literature, very limited information is available on the risk of iron overload with IV iron formulations.	According to section on contraindications in the SmPC, iron(III) isomaltoside 1000 is contraindicated in the following situations: • Iron overload or disturbances in utilisation of iron (e.g. haemocromatosis and haemosiderosis)

Important missing information

Risk	What is known	Preventability
Use in pregnancy and lactation	There are no adequate and well-controlled trials of iron(III) isomaltoside 1000 in pregnant women. A careful risk/benefit evaluation is therefore required before use during pregnancy and iron(III) isomaltoside 1000 should not be used during pregnancy unless clearly necessary. There is no information available on the excretion of iron(III) isomaltoside 1000 in the human breast milk.	Iron deficiency anaemia occurring in the first trimester of pregnancy can in many cases be treated with oral iron. Treatment with iron(III) isomaltoside 1000 should be confined to second and third trimester if the benefit is judged to outweigh the potential risk for both the mother and the foetus. Administration is provided by staff trained to evaluate and manage hypersensitivity reactions and patients are monitoring for early symptoms.

VI.2.5 Summary of additional risk minimisation measures by safety concern

These additional risk minimisation measures are for the following risks:

All medicines have a Summary of Product Characteristics which provides physicians, pharmacists, and other HCPs with details on how to use the medicine, the risks, and recommendations for minimising them.
The Summary of Product Characteristics for MonoFer can be found on www.swissmedicinfo.ch.
This medicine has special conditions and restrictions for its safe and effective use (additional risk minimisation measures). How they are implemented in each country however will depend upon agreement between the manufacturer and the national authorities.
These additional risk minimisation measures are for the following risks:

Allergic Reactions (Hypersensitivity/Anaphylactoid Reaction)

Risk Minimisation Measure(s) – Direct Healthcare Professional Communication and the Checklist
Objective and rationale: The objective is to minimise the risk of serious hypersensitivity reactions based on class label.
Main additional risk minimisation measure: • to inform about the completed referral procedure and its impact on IV iron medicines • to inform about the new class label associated with the IV iron medicines • to inform about the strengthened recommendations for use of IV iron medicines

Use in Pregnant or Lactating Women

Risk Minimisation Measure(s) – Direct Healthcare Professional Communication
Objective and rationale: The objective is to minimise the risk of serious hypersensitivity reactions based on class label.
Main additional risk minimisation measure: • to inform about the completed referral procedure and its impact on IV iron medicines • to inform about the new class label associated with the IV iron medicines • to inform about the strengthened recommendations for use of IV iron medicines

VI.2.6 Planned post authorisation development plan

Study/activity Type, title and category (1-3)	Objectives	Safety concerns addressed	Status	Date for submission of interim or final reports
Joint PASS (Cat. 1)	• Feasibility phase: To evaluate the feasibility of conducting a European multi-country PASS on the utilization and the risk of severe hypersensitivity among users of IV irons products (see synopsis in Annex 6) • PASS: To estimate the utilization and the risk of severe hypersensitivity among users of IV irons products	Hypersensitivity reactions	Oct 2013: IV Iron Consortium established Dec 2014: Feasibility synopsis submitted to PRAC Jul 2015: Response from PRAC to include additional German databases. Sep 2015: IV Iron Consortium submitted response to PRAC recommendations regarding feasibility assessment of IV iron PASS Feb, 2016: IV Iron Consortium informed the PRAC Rapporteur at ANSM and IV Iron consortium that the submission of the report on the PASS feasibility extension to additional German databases would be delayed from March 2016 to June 2016. Final protocol submitted to PRAC in Dec 2016	Feasibility phase: final report by June 2016 (postponed due to extension of feasibility phase) PASS: Final report by 31 July 2017 Postponed – awaits approval by PRAC The final report expected to be end of March 2020

Studies which are a condition of the marketing authorisation

The Joint PASS is a condition of the marketing authorisation.

3. Reference

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[1] Vos T, Flaxman AD, Naghavi M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. The Lancet 2013;380(9859):2163-96.