Annex I

Scientific conclusions and grounds for the variation to the terms of the Marketing Authorisation(s)

Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for iron (parenteral preparations, except for iron dextran), the scientific conclusions are as follows:

Based on the strengths of evidence from spontaneous reports on maternal hypersensitivity reactions, published literature and a possible biological mechanism it is sufficient to conclude on causal relationship of foetal bradycardia with maternal hypersensitivity reactions following the use of intravenous iron containig parenteral preparations. During the hypersensitivity reaction compromised maternal oxygenation may lead to foetal hypoxia that compensatory may result in foetal bradycardia, however other pathophysiological mechanisms cannot be excluded. Therefore, recommendation that the unborn baby should be carefully monitored during intravenous administration of parenteral iron containing medicinal products to pregnant women due to possible occurance of foetal bradycardia as a consequence of a hypersensitivity reaction in the mother should be added in the section 4.6 of the SmPC for all intravenous iron containing medicinal products irrespective of the amount of data regarding foetal bradycardia currently available.

The cumulative weight of evidence from spontaneous reports is sufficient to conclude on causal relationship of superficial thrombophlebitis at injection site with the use of intravenous formulations of sodium ferric gluconate complex. Therefore, the SmPC Section 4.8 for intravenous formulations of medicinal products containing sodium ferric gluconate complex should be updated with adverse drug reaction superficial thrombophlebitis at injection site with frequency "not known". The package leaflet for medicinal products containing intravenous formulations of sodium ferric gluconate complex should be updated accordingly

The CMDh agrees with the scientific conclusions made by the PRAC.

Grounds for the variation to the terms of the Marketing Authorisation(s)

On the basis of the scientific conclusions for iron (parenteral preparations, except for iron dextran) the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing iron (parenteral preparations, except for iron dextran) is unchanged subject to the proposed changes to the product information.

The CMDh reaches the position that the marketing authorisation(s) of products in the scope of this single PSUR assessment should be varied. To the extent that additional medicinal products containing iron (parenteral preparations, except for iron dextran) are currently authorised in the EU or are subject to future authorisation procedures in the EU, the CMDh recommends that the concerned Member States and applicant/marketing authorisation holders take due consideration of this CMDh position.

Annex II

Amendments to the product information of the nationally authorised medicinal product(s)

Amendments to be included in the relevant sections of the Product Information (new text **underlined and in bold**, deleted text ~~strike through~~)

Summary of Product Characteristics

- Section 4.6

The following information should be added for all intravenous iron containing medicinal products:

Foetal bradycardia may occur following administration of parenteral irons. It is usually transient and a consequence of a hypersensitivity reaction in the mother. The unborn baby should be carefully monitored during intravenous administration of parenteral irons to pregnant women.

- Section 4.8

The following information should be added for intravenous formulations of medicinal products containing sodium ferric gluconate complex:

Vascular disorders:
superficial thrombophlebitis at injection site with frequency "not known";

Package Leaflet

- 4. Possible side effects:

Other side effects with unknown frequency:
reactions at the site of injection
vein inflammation causing the formation of a blood clot, symptoms may include red, swollen or painful skin or hardening of the skin at the site of injection.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	July 2019 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	08/09/2019
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	07/11/2019