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:

In view of available data on osteomalacia/hypophosphataemic osteomalacia from the literature and spontaneous reports including data on temporal relationship and in view of a plausible mechanism of action, the PRAC considers a causal relationship between ferric carboxymaltose and hypophosphataemic osteomalacia is at least a reasonable possibility. The PRAC concluded that the product information of products containing ferric carboxymaltose should be amended 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 containing ferric carboxymaltose should be varied. To the extent that additional medicinal products containing containing ferric carboxymaltose 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 4.4

~~*Hypophosphataemia*~~ ***Hypophosphataemic osteomalacia***

~~Parenterally administered iron preparations can cause hypophosphataemia which in most cases is transient and without clinical symptoms~~**Symptomatic** hypophosphataemia **leading to osteomalacia and fractures requiring clinical intervention including surgery**~~medical attention~~ **has been reported in the post marketing setting.**~~, mainly in patients with existing risk factors and after prolonged exposure to high dose intravenous iron.~~**Patients should be asked to seek medical advice if they experience worsening fatigue with myalgias or bone pain. Serum phosphate should be monitored in patients who receive multiple administrations at higher doses or long-term treatment, and those with existing risk factors for hypophosphataemia. In case of persisting hypophosphataemia, treatment with ferric carboxymaltose should be re-evaluated.**

- Section 4.8

~~For subjects in clinical trials that showed a decrease in serum phosphorous, the minimum values were obtained after approximately 2 weeks, and in most cases returned to baseline values by 12 weeks following Ferinject treatment.~~

The following adverse reaction should be added under the SOC Musculoskeletal and connective tissue disorders with a frequency “Not known”:

Hypophosphataemic osteomalacia

Package Leaflet

4. Possible side effects

Serious side effects:

Tell your doctor if you develop worsening of tiredness, muscle or bone pain (pain in your arms or legs, joints or back). That may be a sign of a decrease in blood phosphorus which might cause your bones to become soft (osteomalacia). This condition may sometimes lead to bone fractures. Your doctor may also check the levels of phosphate in your blood, especially if you need a number of treatments with iron over time.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	July 2020 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	6 September 2020
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	5 November 2020