Part VI: Summary of the risk management plan

Summary of risk management plan for FEIBA ([Human Plasma Fraction with FVIII Inhibitor Bypassing Activity])

This is a summary of the risk management plan (RMP) for FEIBA. The RMP details important risks of FEIBA, how these risks can be minimised, and how more informationwill be obtained about FEIBA's risks and uncertainties (missing information).

FEIBA's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how FEIBA should beused.

Important new concerns or changes to the current ones will be included in updates of FEIBA's RMP.

I. The medicine and what it is used for

FEIBA is authorised for control and prevention of bleeding in patients with haemophiliaA (congenital and acquired) and haemophilia B (see the SmPC for the full indication). It contains FVIII Inhibitor Bypassing Activity as the active substance, and it is given IV.

Further information about the evaluation of FEIBA's benefits can be found in FEIBA SmPC.

II. Risks associated with the medicine and activities to minimise or further characterisethe risks

Important risks of FEIBA together with measures to minimise such risks and theproposed studies for learning more about FEIBA's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, inthe package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so toensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g., with or without prescription) can help to minimise its risks.

Together, these measures constitute routine risk minimisation measures.

In addition to these measures, information about ARs is collected continuously and regularly analysed, including PSUR assessment so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilanceactivities.

II.A List of important risks and missing information

Important risks of FEIBA are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns forwhich there is sufficient proof of a link with the use of FEIBA. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g., on the long-term use of the medicine).

List of important risks and missing information	
Important identified risks	Thrombotic and thromboembolic events (including disseminated intravascular coagulation (DIC), myocardial infarction, venous thrombosis, pulmonary embolism, and stroke)
Important potential risks	Thrombotic microangiopathy (TMA) with concomitant emicizumab use

List of important risks and missing information	
Missing information	None

II.B Summary of important risks

Important Identified Risk: Thrombotic and thromboembolic events (including disseminated intravascular coagulation (DIC), myocardial infarction,venous thrombosis, pulmonary embolism, and stroke)	
Evidence for linking the risk to the medicine	Thrombotic and TEEs are a known complication with FEIBA and have been seen in the post-marketing setting. The risk increases with high doses of FEIBA.
Risk factors and risk groups	Patients with one or more co-suspect medication (e.g., rFVIIa, tranexamicacid, other blood derived products or drugs with thrombogenic potential). Inhibitor development in patients with acquired haemophilia is thought to result from underlying medical conditions. Some of the medical conditionsassociated with the development of inhibitors are known to be associated with an increased risk of thrombosis. Sequential or combined treatment of bleeds in acquired haemophilia as well as in congenital haemophilia where inhibitors appears to increase therisk of thrombotic complications. Pre-disposing co-morbidities and risk factors, for example, advanced age,severe injury, hypertension, diabetes, and immobility. DIC, MI, stroke, venous thrombosis, pulmonary embolism, and MI were also found to occur after receiptof a dose exceeding the recommended maximum daily dose and/or prolonged administration.
Risk minimisation measures	**Routine risk minimisation measures:** SmPC Sections: 4.3 Contraindications 4.4 Special warnings and the precautions for use 4 8 Undesirable effects 4.9 Overdose **Additional risk minimisation measures:** None

Important Potential Risk: Thrombotic microangiopathy (TMA) withconcomitant emicizumab use	
Evidence for linking the risk to the medicine	TMA has not been reported in Company sponsored studies with FEIBA TMA was reported in one emicizumab trial where FEIBA was part of a treatment regimen for breakthrough bleeding.
Risk factors and risk groups	With concomitant use of emicizumab.
Risk minimisation measures	**Routine risk minimisation measures:** SmPC Sections: 4.4 Special warnings and the precautions for use 4.5 Interactions with other medicinal products and other forms of

Important Potential Risk: Thrombotic microangiopathy (TMA) withconcomitant emicizumab use	
	interaction **Additional risk minimisation measures:** None

II.C. Post-authorisation development plan

II.C.1. Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of FEIBA.

II.C.2. Other studies in post-authorisation development plan

There are no studies required for FEIBA.