Summary of risk management plan for ReFacto AF (moroctocog alfa [AF-CC])

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

ReFacto AF's Summary of Product Characteristics (SmPC) and its Package Leaflet (PL) give essential information to healthcare professionals and patients on how ReFacto AF should be used.

This summary of the RMP for ReFacto AF should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

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

I. The Medicine and What It Is Used For

ReFacto AF is authorised for the treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency). ReFacto AF is appropriate for use in adults and children of all ages, including newborns. ReFacto AF does not contain von Willebrand factor, and hence is not indicated in von Willebrand's disease. It contains moroctocog alfa (AF-CC) as the active substance and it is given by intravenous injection.

Further information about the evaluation of ReFacto AF's benefits can be found in ReFacto AF's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/000232/human_med_001019.jsp&mid=WC0b01ac058001d124

II. Risks Associated With the Medicine and Activities to Minimise or Further Characterise the Risks

Important risks of ReFacto AF, together with measures to minimise such risks and the proposed studies for learning more about ReFacto AF'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, in the 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 to ensure that the medicine is used correctly;

- The medicine's legal status — the way a medicine is supplied to the public (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 adverse events is collected continuously and regularly analysed, including PSUR assessment, so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

If important information that may affect the safe use of ReFacto AF is not yet available, it is listed under 'missing information' below.

II.A. List of Important Risks and Missing Information

Important risks of ReFacto AF 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 for which there is sufficient proof of a link with the use of ReFacto AF. 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 (eg, on the long-term use of the medicine).

Table 1. List of important risks and missing information

Important identified risks	Inhibitor development Allergic reactions
Important potential risks	Medication error/product confusion
Missing information	None

II.B. Summary of Important Risks and Missing Information

Table 2. Important Identified Risk: Inhibitor Development

Evidence for linking the risk to the medicine	CT and postmarketing data.
Risk factors and risk groups	Inhibitor development is an inherent risk with all FVIII products. Inhibitors are more common in severe haemophilia A and are uncommon in patients with mild to moderate haemophilia. Additional factors that may affect the risk of the inhibitor development include: • Severe haemophilia caused by mutations associated with a major loss of coding information (eg, large deletions, inversions and mutations which result in premature translation stops). • Family history of inhibitor development. • Number of previous exposure days to FVIII; PUPs are at substantially greater risk than PTPs. • Certain ethnic groups, eg, those of African ancestry. • The presence of factors such as intensive treatment and/or severe illness during FVIII administration.
Risk minimisation measures	Routine risk minimisation measures: SmPC Sections 4.4, 4.8, and 5.1; PL Sections 2 and 4. Additional risk minimisation measures: None

Table 3. Important Identified Risk: Allergic Reactions

Evidence for linking the risk to the medicine	CT and postmarketing data.
Risk factors and risk groups	No clinically important subpopulation differences in risk were identified other than patients with a noted past hypersensitivity to the active substance or any of the excipients or patients with known allergic reactions to hamster proteins who are at increased risk for allergic type hypersensitivity reactions. Previously untreated patients (PUPs) with severe haemophilia A treated with any FVIII replacement therapy may be more susceptible to an allergic reaction compared with PTPs.
Risk minimisation measures	Routine risk minimisation measures: SmPC Sections 4.3, 4.4, and 4.8; PL Sections 2 and 4. Additional risk minimisation measures: None

Table 4. Important Potential Risk: Medication Error/Product Confusion

Evidence for linking the risk to the medicine	Postmarketing data.
Risk factors and risk groups	No clinically important subpopulation differences in risk were identified.
Risk minimisation measures	Routine risk minimisation measures: SmPC Sections 6.2, 6.3, 6.4, 6.5, and 6.6; PL Sections 3, 5, and 6 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 ReFacto AF.

II.C.2. Other Studies in Post-Authorisation Development Plan

There are no studies required for ReFacto AF.