Summary of risk management plan for Elocta (efmoroctocog alfa)

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

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

This summary of the RMP for Elocta 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 Elocta's RMP.

I. The medicine and what it is used for

Elocta is authorised for treatment and prophylaxis of bleeding in patients with hemophilia A (congenital factor VIII deficiency). Elocta can be used for all age groups (see SmPC for the full indication). It contains efmoroctocog alfa (recombinant coagulation factor VIII Fc fusion protein) as the active substance and it is given by intravenous injection.

Further information about the evaluation of Elocta's benefits can be found in Elocta's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage.

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

Important risks of Elocta, together with measures to minimise such risks and the proposed studies for learning more about Elocta'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 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 adverse reactions 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 Elocta is not yet available, it is listed under 'missing information' below.

II.A. List of important risks and missing information

Important risks of Elocta 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 Elocta. 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	Inhibitor development to factor VIII
Important potential risks	Serious vascular thromboembolic events
Missing information	None

II.B. Summary of important risks

Important identified risk: Inhibitor development to factor VIII	
Evidence for linking the risk to the medicine	This is a known risk for FVIII replacement therapy, including Elocta. Inhibitor development have been observed in the completed study in previously untreated patients (Study 997HA306) and in the postmarketing setting.
Risk factors and risk groups	The causes of inhibitor development to FVIII are not known. The risk has been associated with peak treatment moments, surgery, family history of inhibitors, and FVIII genetic mutation, including large deletions, nonsense mutations, or intron 22 inversions.
Risk minimisation measures	Routine risk communication: • SmPC section 4.8 • PL section 4 Routine risk minimisation activities recommending specific clinical measures to address the risk: • Recommendation for monitoring development of inhibitors by appropriate clinical observation and laboratory tests are included in SmPC sections 4.4 • How to detect early signs and symptoms of inhibitor development in PL section 2 Other routine risk minimisation measures beyond the Product Information**:** None Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • European Haemophilia Safety Surveillance System (EUHASS) participation and data collection See section II.C of this summary for an overview of the post-authorisation development plan.

Important potential risk: Serious vascular thromboembolic events	
Evidence for linking the risk to the medicine	In the literature, thrombotic events reported in hemophilia A patients treated with FVIII replacement products are rare. The risk of vascular thromboembolic events with the use recombinant factor VIII products, such as Elocta, has not been established. Published reports of vascular thrombotic adverse events in patients with hemophilia A and recombinant FVIII replacement occur in the setting of pre-existing risk factors, e.g. cardiovascular risk factors and indwelling central venous catheters.
Risk factors and risk groups	Patients with pre-existing risk factors for thromboembolism (e.g. cardiovascular risk factors, indwelling central venous catheters). Cardiovascular risk factors are more likely to occur with advancing age.
Risk minimisation measures	Routine risk communication:None Routine risk minimisation activities recommending specific clinical measures to address the risk: • Information about risk of cardiovascular events in patient with existing cardiovascular risk factors is included in SmPC section 4.4 • Information about risk of catheter-related complications, including catheter site thrombosis is included in SmPC section 4.4 • Information about risk of catheter-related complications, including catheter site thrombosis is described in PL Section 2 Other routine risk minimisation measures beyond the Product Information: None Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • European Haemophilia Safety Surveillance System (EUHASS) participation and data collection See section II.C of this summary for an overview of the post-authorisation development plan.

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 Elocta.

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

- Data collection from participation in the European Haemophilia Safety Surveillance System (EUHASS) registry.
  Purpose of the study: To monitor the treatment safety of hemophilia A.