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Summary of the risk management plan (RMP) for Elocta (efmoroctocog alfa)

This is a summary of the risk management plan (RMP) for Elocta, which details the measures to be taken in order to ensure that Elocta is used as safely as possible. For more information on RMP summaries, see here.

This RMP summary should be read in conjunction with the EPAR summary and the product information for Elocta, which can be found on Elocta's EPAR page.

Overview of disease epidemiology

Elocta is used to treat and prevent bleeding in patients with haemophilia A (an inherited bleeding disorder caused by lack of factor VIII).

Haemophilia A occurs predominantly in males, affecting about 1 in 5,000 male births. Worldwide, about 142,000 people are reported to have haemophilia A. Of these, about 33,000 cases are in the European Union, with similar rates across racial and ethnic groups.

Haemophilia A is caused by mutations in the *FVIII* gene. About 70% of cases are inherited mutations, while in 30% of cases there is no family history of the condition. Individuals with severe haemophilia experience spontaneous and/or prolonged bleeding; bleeding into the joints causes joint pain and severe disability.

Common comorbidities include human immunodeficiency virus (HIV) infection, hepatitis C, other infections, and chronic joint disease. With adequate treatment, life expectancy of patients approaches average life expectancy for men.

Summary of treatment benefits

Two main studies of Elocta showed that the medicine is effective at both preventing and treating bleeding episodes.

In a study of 165 adult patients with haemophilia A, patients who were given Elocta as a tailored preventive treatment had around 3 bleeding episodes a year, which compares with 37 episodes a year in patients not given preventive treatment. In addition, when bleeding did occur, Elocta treatment was rated as 'excellent' or 'good' in more than 78% of cases, with 87% of bleeding episodes resolving with only one injection.

In a study in 69 children, Elocta was similarly effective: 2 bleeding episodes occurred per year on average and 81% of bleeding episodes resolved with only one injection.

Unknowns relating to treatment benefits

Most people who received Elocta in the clinical studies were Caucasian, but other races were represented and no differences were observed across the race subgroups. It is likely that Elocta will work well in people of all races and ethnicities.

Information from clinical studies on the use of Elocta in patients 65 years of age and older, in children under 2 years of age and in patients with kidney insufficiency or with risk factors for thromboembolic (clotting) events is limited. Information from Elocta clinical studies on previously untreated patients with haemophilia A is not yet available. Information on Elocta use for immune tolerance induction (ITI) is not yet available. A study (Study 997HA306), which is in progress, is looking at Elocta treatment in previously untreated patients, including use in ITI (see section on Planned post-authorisation development plan).

There is no experience with Elocta in pregnant or breastfeeding women.

Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Inhibitor development	The formation of neutralising antibodies (inhibitors) to factor VIII is a known complication in the management of individuals with haemophilia A and can prevent the treatment from working properly.	Patients should be carefully monitored for the development of inhibitors. In patients with high levels of inhibitors, treatment with factor VIII may not be effective and alternative treatment should be considered.

Important potential risks

Risk	What is known
Hypersensitivity or anaphylactic reaction	Hypersensitivity (allergic) reactions have been reported with factor VIII replacement therapy products and are possible with Elocta. The signs of hypersensitivity reactions may include swelling of the face, rash, hives, tightness of the chest, and difficulty breathing. If signs of hypersensitivity reactions occur, patients should stop treatment with Elocta and contact their doctor.
Complications of abnormal blood clot formation	Blood clots that may block blood vessels have been reported with factor VIII products. The risk of blood clots with the use recombinant factor VIII products such as Elocta has not been established.
Medication errors	Elocta is available as a freeze-dried powder in single-use vials containing 250, 500, 750, 1000, 1500, 2000, or 3000 international units (IU) per vial. Although there is a potential for error, the package leaflet clearly describes how the medicine should be given. Colour coding of the different vial strengths will further prevent medication errors.

Missing information

Risk	What is known
Safety profile in patients aged	The number of patients aged 65 years or older treated with Elocta to date is too limited to establish the safety profile of Elocta in this group.

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65 years or older	
Safety profile in patients with renal (kidney) insufficiency	Information in the clinical studies on the use of Elocta in patients with renal insufficiency is limited so the complete safety profile of Elocta in this group cannot yet be determined.
Safety profile in children aged below 2 years old	The number of children aged below 2 years old treated with Elocta to date is too limited to determine the complete safety profile of Elocta in this group.
Safety profile in previously untreated patients	The number of previously untreated patients treated with Elocta is limited at this time, so the complete safety profile of Elocta in this group cannot yet be determined. Study 997HA306 to assess the safety of Elocta in previously untreated patients is ongoing.
Use of Elocta for immune tolerance induction	The use of Elocta in immune tolerance induction therapy to eradicate inhibitors to factor VIII has not yet been established.
Use in female patients (including pregnant and breastfeeding women)	No information regarding women, including pregnant and breastfeeding women, treated with Elocta is currently available, so the complete safety profile of Elocta in this group cannot yet be determined.

Summary of risk minimisation measures by safety concern

All medicines have a summary of product characteristics (SmPC) which provides physicians, pharmacists and other healthcare professionals with details on how to use the medicine, and also describes the risks and recommendations for minimising them. Information for patients is available in lay language in the package leaflet. The measures listed in these documents are known as 'routine risk minimisation measures'.

The SmPC and the package leaflet are part of the medicine's product information. The product information for Elocta can be found on Elocta's EPAR page.

This medicine has no additional risk minimisation measures.

Planned post-authorisation development plan

List of studies in post-authorisation development plan

Study / activity (including study number)	Objectives	Safety concerns / efficacy issue addressed	Status	Planned date for submission of (interim and) final results
8HA01EXT, An open-label, multicentre evaluation of the long-term safety and efficacy of recombinant	The primary objective of the study is to evaluate the long-term	Long-term safety evaluation. Safety profile in patients aged	Ongoing	Submission date dependent on study finish dates. Study last patient last visit by March

Study / activity (including study number)	Objectives	Safety concerns / efficacy issue addressed	Status	Planned date for submission of (interim and) final results
human coagulation factor VIII fusion protein (rFVIIIFc) in the prevention and treatment of bleeding episodes in previously treated subjects with haemophilia A (safety extension study)	safety of Elocta in subjects with haemophilia A	65 years or older		2017 as per the agreed PIP (EMEA-001114-PIP01-10-M02)
997HA306, An open-label, multicentre evaluation of the safety and efficacy of recombinant coagulation factor VIII Fc fusion protein (rFVIIIFc; BIIB031) in the prevention and treatment of bleeding in PUPs with severe haemophilia A (PUPs study)	The primary objective of the study is to evaluate the safety of Elocta in previously untreated patients with severe haemophilia A	Safety profile in previously untreated patients including patients less than 2 years old	Ongoing	Submission date dependent on study finish dates. Study last patient last visit by September 2019 as per agreed PIP (EMEA-001114-PIP01-10-M02)
997HA307, Crossover study to investigate the PK of the 1000 and 3000 IU/ vial strengths. Phase 3	The primary objective of the study is to characterize the pharmacokinetics of Elocta administered at doses of 1000 and 3000 IU in subjects with severe haemophilia A.	Safety of Elocta beyond the Pharmacokinetic assessment for up to 6 months	Ongoing	May 2016
Data collected from participation in the European Haemophilia Safety Surveillance System (EUHASS) registry to be provided on an ongoing basis	Monitor the safety of treatments for people with haemophilia, including with Elocta.	Inhibitor development Serious allergic reactions or anaphylaxis Serious vascular thrombotic events	Planned – will start upon product launch in the EU	Data will be reviewed on an ongoing basis as a part of Pharmacovigilance signal detection and reported within the PSUR reports

Studies which are a condition of the marketing authorisation

None of the above studies are conditions of the marketing authorisation.

Summary of changes to the risk management plan over time

Not applicable.

This summary was last updated in 10-2015.