

ANNEX I
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

ELOCTA 250 IU powder and solvent for solution for injection

ELOCTA 500 IU powder and solvent for solution for injection

ELOCTA 750 IU powder and solvent for solution for injection

ELOCTA 1000 IU powder and solvent for solution for injection

ELOCTA 1500 IU powder and solvent for solution for injection

ELOCTA 2000 IU powder and solvent for solution for injection

ELOCTA 3000 IU powder and solvent for solution for injection

ELOCTA 4000 IU powder and solvent for solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ELOCTA 250 IU powder and solvent for solution for injection

Each vial contains nominally 250 IU efmoctocog alfa.

ELOCTA contains approximately 83 IU/mL of recombinant human coagulation factor VIII, efmoctocog alfa after reconstitution.

ELOCTA 500 IU powder and solvent for solution for injection

Each vial contains nominally 500 IU efmoctocog alfa. ELOCTA contains approximately 167 IU/mL of recombinant efmoctocog alfa after reconstitution.

ELOCTA 750 IU powder and solvent for solution for injection

Each vial contains nominally 750 IU efmoctocog alfa. ELOCTA contains approximately 250 IU/mL of recombinant efmoctocog alfa after reconstitution.

ELOCTA 1000 IU powder and solvent for solution for injection

Each vial contains nominally 1000 IU efmoctocog alfa. ELOCTA contains approximately 333 IU/mL of recombinant efmoctocog alfa after reconstitution.

ELOCTA 1500 IU powder and solvent for solution for injection

Each vial contains nominally 1500 IU efmoctocog alfa. ELOCTA contains approximately 500 IU/mL of recombinant efmoctocog alfa after reconstitution.

ELOCTA 2000 IU powder and solvent for solution for injection

Each vial contains nominally 2000 IU efmoctocog alfa. ELOCTA contains approximately 667 IU/mL of recombinant efmoctocog alfa after reconstitution.

ELOCTA 3000 IU powder and solvent for solution for injection

Each vial contains nominally 3000 IU efmoctocog alfa. ELOCTA contains approximately 1000 IU/mL of recombinant efmoctocog alfa after reconstitution.

ELOCTA 4000 IU powder and solvent for solution for injection

Each vial contains nominally 4000 IU efmoctocog alfa. ELOCTA contains approximately 1333 IU/mL of recombinant efmoctocog alfa after reconstitution.

The potency (International Units (IU)) is determined using the European Pharmacopoeia chromogenic assay. The specific activity of ELOCTA is 4000-10200 IU/mg protein.

Efmoroctocog alfa (recombinant human coagulation factor VIII, Fc fusion protein (rFVIII_{Fc})) has 1,890 amino acids. It is produced by recombinant DNA technology in a human embryonic kidney (HEK) cell line without the addition of any exogenous human- or animal-derived protein in the cell culture process, purification or final formulation.

Excipient with known effect

0.6 mmol (or 14 mg) sodium per vial.

0.4 mg of polysorbate 20 per vial.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and solvent for solution for injection.

Powder: lyophilised, white to off-white powder or cake.

Solvent: water for injections, a clear, colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency).

ELOCTA can be used for all age groups.

4.2 Posology and method of administration

Treatment should be initiated under the supervision of a physician experienced in the treatment of haemophilia.

Treatment monitoring

During the course of treatment, appropriate determination of factor VIII levels (by one-stage clotting or chromogenic assays) is advised to guide the dose to be administered and the frequency of repeated injections. Individual patients may vary in their response to factor VIII, demonstrating different half-lives and recoveries. Dose based on bodyweight may require adjustment in underweight and overweight patients. In the case of major surgical interventions in particular, precise monitoring of the substitution therapy by means of coagulation analysis (plasma factor VIII activity) is indispensable.

When using an *in vitro* thromboplastin time (aPTT)-based one stage clotting assay for determining factor VIII activity in patients' blood samples, plasma factor VIII activity results can be significantly affected by both the type of the aPTT reagent and the reference standard used in the assay. Also there can be significant discrepancies between assay results obtained by aPTT-based one stage clotting assay and the chromogenic assay according to Ph. Eur. This is of importance particularly when changing the laboratory and/or reagent used in the assay.

Posology

The dose and duration of the substitution therapy depend on the severity of the factor VIII deficiency, on the location and extent of the bleeding and on the patient's clinical condition.

The number of units of factor VIII administered is expressed in IU, which are related to the current WHO standard for factor VIII products. Factor VIII activity in plasma is expressed either as a percentage (relative to normal human plasma) or in IU (relative to an International Standard for factor VIII in plasma).

One IU of recombinant factor VIII Fc activity is equivalent to that quantity of factor VIII in one mL of normal human plasma.

On-demand treatment

The calculation of the required dose of recombinant factor VIII Fc is based on the empirical finding that 1 IU factor VIII per kg body weight raises the plasma factor VIII activity by 2 IU/dL. The required dose is determined using the following formula:

$$\text{Required units} = \text{body weight (kg)} \times \text{desired factor VIII rise (\% (IU/dL)} \times 0.5 \text{ (IU/kg per IU/dL)}$$

The amount to be administered and the frequency of administration should always be oriented to the clinical effectiveness in the individual case.

In the case of the following haemorrhagic events, the factor VIII activity should not fall below the given plasma activity level (in % of normal or IU/dL) in the corresponding period. Table 1 can be used to guide dosing in bleeding episodes and surgery:

Table 1: Guide to ELOCTA dosing for treatment of bleeding episodes and surgery

Degree of haemorrhage / Type of surgical procedure	Factor VIII level required (%) (IU/dL)	Frequency of doses (hours)/ Duration of therapy (days)
<u>Haemorrhage</u>		
Early haemarthrosis, muscle bleeding or oral bleeding	20-40	Repeat injection every 12 to 24 hours for at least 1 day, until the bleeding episode as indicated by pain is resolved or healing is achieved. ¹
More extensive haemarthrosis, muscle bleeding or haematoma	30-60	Repeat injection every 12 to 24 hours for 3-4 days or more until pain and acute disability are resolved. ¹
Life threatening haemorrhages	60-100	Repeat injection every 8 to 24 hours until threat is resolved.
<u>Surgery</u>		
Minor surgery including tooth extraction	30-60	Repeat injection every 24 hours, for at least 1 day, until healing is achieved.
<u>Major surgery</u>	80-100 (pre- and post-operative)	Repeat injection every 8 to 24 hours as necessary until adequate wound healing, then therapy at least for another 7 days to maintain a factor VIII activity of 30% to 60% (IU/dL).

¹ In some patients and circumstances the dosing interval can be prolonged up to 36 hours. See section 5.2 for pharmacokinetic data.

Prophylaxis

For long term prophylaxis, the recommended dose is 50 IU of factor VIII per kg body weight at intervals of 3 to 5 days. The dose may be adjusted based on patient response in the range of 25 to 65 IU/kg (see section 5.1 and 5.2).

In some cases, especially in younger patients, shorter dosage intervals or higher doses may be necessary.

Elderly

There is limited experience in patients ≥65 years.

Paediatric population

For children below the age of 12, more frequent or higher doses may be required (see section 5.1). For adolescents of 12 years of age and above, the dose recommendations are the same as for adults.

Method of administration

ELOCTA is for intravenous use.

ELOCTA should be injected intravenously over several minutes. The rate of administration should be determined by the patient's comfort level and should not exceed 10 mL/min.

For instructions on reconstitution of the medicinal product before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Hypersensitivity

Allergic type hypersensitivity reactions are possible with ELOCTA. If symptoms of hypersensitivity occur, patients should be advised to discontinue use of the medicinal product immediately and contact their physician. Patients should be informed of the signs of hypersensitivity reactions including hives, generalised urticaria, tightness of the chest, wheezing, hypotension and anaphylaxis.

In case of shock, standard medical treatment for shock should be implemented.

Inhibitors

The formation of neutralising antibodies (inhibitors) to factor VIII is a known complication in the management of individuals with haemophilia A. These inhibitors are usually IgG immunoglobulins directed against the factor VIII procoagulant activity, which are quantified in Bethesda Units (BU) per mL of plasma using the modified assay. The risk of developing inhibitors is correlated to the severity of the disease as well as the exposure to factor VIII, this risk being highest within the first 50 exposure days but continues throughout life although the risk is uncommon.

The clinical relevance of inhibitor development will depend on the titre of the inhibitor, with low titre posing less of a risk of insufficient clinical response than high titre inhibitors.

In general, all patients treated with coagulation factor VIII products should be carefully monitored for the development of inhibitors by appropriate clinical observations and laboratory tests. If the expected factor VIII activity plasma levels are not attained, or if bleeding is not controlled with an appropriate dose, testing for factor VIII inhibitor presence should be performed. In patients with high levels of inhibitor, factor VIII therapy may not be effective and other therapeutic options should be considered. Management of such patients should be directed by physicians with experience in the care of haemophilia and factor VIII inhibitors.

Cardiovascular events

In patients with existing cardiovascular risk factors, substitution therapy with FVIII may increase the cardiovascular risk.

Catheter-related complications

If a central venous access device (CVAD) is required, risk of CVAD-related complications including local infections, bacteraemia and catheter site thrombosis should be considered.

Traceability

In order to improve traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Paediatric population

The listed warnings and precautions apply both to adults, children and adolescents.

Excipient related considerations

Sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium-free'.

However, depending on the body weight and posology, the patient could receive more than one vial (see section 2 for information on content per vial). This should be taken into consideration by patients on a controlled sodium diet.

Polysorbate

This medicine contains 0.4 mg of polysorbate 20 in each vial. Polysorbates may cause allergic reactions.

4.5 Interaction with other medicinal products and other forms of interaction

No interactions of human coagulation factor VIII (rDNA) with other medicinal products have been reported. No interaction studies have been performed.

4.6 Fertility, pregnancy and lactation

Animal reproduction studies have not been conducted with factor VIII. A placental transfer study in mice was conducted with ELOCTA (see section 5.3). Based on the rare occurrence of haemophilia A in women, experience regarding the use of factor VIII during pregnancy and breast-feeding is not available. Therefore, factor VIII should be used during pregnancy and breast-feeding only if clearly indicated.

4.7 Effects on ability to drive and use machines

ELOCTA has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

Hypersensitivity or allergic reactions (which may include angioedema, burning and stinging at the infusion site, chills, flushing, generalised urticaria, headache, hives, hypotension, lethargy, nausea, restlessness, tachycardia, tightness of the chest, tingling, vomiting, wheezing) have been observed rarely and may in some cases progress to severe anaphylaxis (including shock).

Development of neutralising antibodies (inhibitors) may occur in patients with haemophilia A treated with factor VIII, including with ELOCTA. If such inhibitors occur, the condition will manifest itself as an insufficient clinical response. In such cases, it is recommended that a specialised haemophilia centre be contacted.

Tabulated list of adverse reactions

The Table 2 presented below is according to the MedDRA system organ classification (SOC and Preferred Term Level). Frequencies of adverse reactions are based on clinical studies with a total of 379 patients with severe haemophilia A, of which 276 were previously treated patients (PTPs) and 103 were previously untreated patients (PUPs). See section 5.1 for additional details on the clinical studies.

Frequencies have been evaluated according to the following convention: very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1,000$ to $< 1/100$); rare ($\geq 1/10,000$ to $< 1/1,000$); very rare ($< 1/10,000$), not known (cannot be estimated from the available data).

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 2: Adverse reactions reported for ELOCTA in clinical trials¹

MedDRA System Organ Class	Adverse reactions	Frequency category ¹
Blood and lymphatic system disorders	FVIII inhibition	Uncommon (PTPs) ² Very common (PUPs) ²
Nervous system disorders	Headache	Uncommon
	Dizziness	Uncommon
	Dysgeusia	Uncommon
Cardiac disorders	Bradycardia	Uncommon
Vascular disorders	Hypertension	Uncommon
	Hot flush	Uncommon
	Angiopathy ⁴	Uncommon
Respiratory, thoracic, and mediastinal disorders	Cough	Uncommon
Gastrointestinal disorders	Abdominal pain, lower	Uncommon
Skin and subcutaneous tissue disorders	Papular rash	Common (PUPs) ³
	Rash	Uncommon
Musculoskeletal and connective tissue disorders	Arthralgia	Uncommon
	Myalgia	Uncommon
	Back pain	Uncommon
	Joint swelling	Uncommon
General disorders and administration site conditions	Device related thrombosis	Common (PUPs) ³
	Malaise	Uncommon
	Chest pain	Uncommon
	Feeling cold	Uncommon
	Feeling hot	Uncommon
Injury, poisoning, and procedural complications	Procedural hypotension	Uncommon

PTPs = previously treated patients, PUPs = previously untreated patients.

¹ ADRs and frequency are based on occurrence in PTPs only, unless otherwise noted.

² Frequency is based on studies with all FVIII products which included patients with severe haemophilia A.

³ ADRs and frequency are based on occurrence in PUPs only.

⁴ Investigator term: *vascular pain after injection of ELOCTA*.

Paediatric population

No age-specific differences in adverse reactions were observed between paediatric and adult subjects. Frequency, type and severity of adverse reactions in children are expected to be the same as in adults.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in [Appendix V](#).

4.9 Overdose

No symptoms of overdose have been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antihemorrhagics, blood coagulation factor VIII, ATC code: B02BD02

Mechanism of action

The factor VIII/von Willebrand factor complex consists of two molecules (factor VIII and von Willebrand factor) with different physiological functions. When infused into a haemophiliac patient, factor VIII binds to von Willebrand factor in the patient's circulation. Activated factor VIII acts as a cofactor for activated factor IX, accelerating the conversion of factor X to activated factor X. Activated factor X converts prothrombin into thrombin. Thrombin then converts fibrinogen into fibrin and a clot can be formed.

Haemophilia A is an X-linked hereditary disorder of blood coagulation due to decreased levels of functional factor VIII:C and results in bleeding into joints, muscles or internal organs, either spontaneously or as a result of accidental or surgical trauma. By replacement therapy the plasma levels of factor VIII are increased, thereby enabling a temporary correction of the factor deficiency and correction of the bleeding tendencies.

Of note, annualized bleeding rate (ABR) is not comparable between different factor concentrates and between different clinical studies.

ELOCTA (efmoroctocog alfa) is a fully recombinant fusion protein with extended half-life. ELOCTA is comprised of recombinant B-domain deleted human coagulation factor VIII covalently linked to the Fc domain of human immunoglobulin G1. The Fc region of human immunoglobulin G1 binds to the neonatal Fc receptor. This receptor is expressed throughout life and is part of a naturally occurring pathway that protects immunoglobulins from lysosomal degradation by cycling these proteins back into circulation, resulting in their long plasma half-life. Efmoroctocog alfa binds to neonatal Fc receptor thereby utilising this same naturally occurring pathway to delay lysosomal degradation and allow for longer plasma half-life than endogenous factor VIII.

Clinical efficacy and safety

The safety, efficacy, and pharmacokinetics of ELOCTA in previously treated patients (PTPs) were evaluated in 2 multinational, open-label, pivotal phase 3 studies, Study I and Study II (see Paediatric population), and an extension study (Study III) with a duration of up to four years. In total 276 PTPs were followed for a total of 80,848 exposure days with a median of 294 (range 1-735) exposure days per patient. In addition, a phase 3 study (Study IV) was performed to evaluate the safety and efficacy of ELOCTA in previously untreated patients (PUPs) (see Paediatric population).

Study I enrolled 165 previously treated male patients (12 to 65 years of age) with severe haemophilia A. Subjects on prophylaxis regimens prior to entering the study were assigned to the individualised prophylaxis arm. Subjects on on-demand therapy prior to entry either entered the individualised prophylaxis arm or were randomised to the weekly prophylaxis or on-demand arms.

Prophylaxis regimens:

Individualised prophylaxis: 25 to 65 IU/kg every 3 to 5 days.

Weekly prophylaxis: 65 IU/kg

Out of 153 subjects who completed Study I, 150 were enrolled onto Study III (extension study). Median total time on Study I+III was 4.2 years and median number of exposure days was 309.

Individualised prophylaxis: Median annual factor consumption was 4212 IU/kg (min. 2877, max. 7943) in Study I and 4223 IU/kg (min. 2668, max 8317) in Study III. Respective median Annualized Bleed Rate (ABR) was 1.60 (min. 0, max. 18.2) and 0.74 (min. 0, max. 15.6).

Weekly prophylaxis: Median annual factor consumption was 3805 IU/kg (min. 3353, max. 6196) in Study I and 3510 IU/kg (min. 2758, max. 3984) in Study III. Respective median ABR was 3.59 (min. 0, max. 58.0) and 2.24 (min. 0, max. 17.2).

On-demand treatment: Median annual factor consumption was 1039 IU/kg (min. 280, max. 3571) for 23 patients randomised to the on-demand treatment arm in Study I and 671 IU/kg (min. 286, max. 913) for 6 patients remaining on on-demand treatment for at least one year in Study III.

Subjects that switched from on-demand treatment to weekly prophylaxis during Study III had a median ABR of 1.67.

Treatment of bleeding: 2490 bleeding events were treated during Study I and III with a median dose of 43.8 IU/kg (min. 13.0, max. 172.8) to control each bleed. 79.2 % of first injections were rated as excellent or good by the patients.

Perioperative management (surgical prophylaxis): A total of 48 major surgical procedures were performed and assessed in 34 subjects in Study I and Study III. The haemostatic response was rated by the physicians as excellent in 41 and as good in 3 of 44 major surgeries. Median dose to maintain haemostasis during surgery was 60.6 IU/kg (min. 38, max. 158).

Paediatric population

Study II enrolled a total of 71 previously treated male paediatric patients <12 years of age with severe haemophilia A. Of the 71 enrolled subjects, 69 received at least 1 dose of ELOCTA and were evaluable for efficacy (35 were <6 years of age and 34 were 6 to <12 years of age). The starting prophylactic regimen consisted of 25 IU/kg on the first day followed by 50 IU/kg on the fourth day. Dosing of up to 80 IU/kg and a dosing interval as short as 2 days was allowed and used in a limited number of patients. Out of 67 subjects having completed Study II, 61 enrolled onto Study III (extension study). Median total time on study II+III was 3.4 years and median number of exposure days was 332.

Prophylaxis, age <6 years: Median dose interval was 3.50 days in Study II and Study III. Median annual factor consumption was 5146 IU/kg (min. 3695, max. 8474) in Study II and 5418 IU/kg (min. 3435, max. 9564) in Study III. Respective median Annualized Bleed Rate (ABR) was 0.00 (min. 0, max. 10.5) and 1.18 (min. 0, max. 9.2).

Prophylaxis, age 6 up to 12 years: Median dose interval was 3.49 days in Study II and 3.50 days in Study III. Median annual factor consumption was 4700 IU/kg (min. 3819, max. 8230 IU/kg) in Study II and 4990 IU/kg (min. 3856, max. 9527) in Study III. Respective median ABR was 2.01 (min. 0, max. 27.2) and 1.59 (min. 0, max. 8.0).

12 adolescent subjects age 12 up to 18 years were included in the adult study population on prophylactic treatment. Median annual factor consumption was 5572 IU/kg (min. 3849, max. 7035) in Study I and 4456 IU/kg (min. 3563, max. 8011) in Study III. Respective median ABR was 1.92 (min. 0, max. 7.1) and 1.25 (min. 0, max. 9.5).

Treatment of bleeding: During Studies II and III, 447 bleeding events were treated with a median dose of 63 IU/kg (min. 28, max. 186) to control each bleed. 90.2 % of first injections were rated as excellent or good by the patients and their caregivers.

Study IV evaluated 103 male previously untreated patients (PUPs) <6 years of age with severe haemophilia A. Patients were followed for a total of 11,255 exposure days with a median of 100 (range 0-649) exposure days per patient. Most subjects started on episodic treatment (N=81) with subsequent transition to prophylaxis (N=69). At any time during the study, 89 PUPs received prophylaxis. The recommended initial dose on prophylaxis was 25–80 IU/kg at 3–5-day intervals. For subjects on prophylaxis, the median average weekly dose was 101.4 IU/kg (range: 28.5-776.3 IU/kg) and the median dosing interval was 3.87 days (range 1.1 to 7 days). Median annual factor consumption was 3971.4 IU/kg. Annualized Bleeding Rate was 1.49 (min. 0.0, max. 18.7).

5.2 Pharmacokinetic properties

All pharmacokinetic studies with ELOCTA were conducted in previously treated patients with severe haemophilia A. Data presented in this section were obtained by chromogenic and one-stage clotting assays. The pharmacokinetic parameters from the chromogenic assay data were similar to those derived for the one-stage assay.

Pharmacokinetic properties were evaluated in 28 subjects (≥ 15 years) receiving ELOCTA (rFVIII-Fc). Following a washout period of at least 96 hours (4 days), the subjects received a single dose of 50 IU/kg of ELOCTA. Pharmacokinetic samples were collected pre-dose and then subsequently at 7 time points up to 120 hours (5 days) post-dose. Pharmacokinetic parameters after 50 IU/kg dose of ELOCTA are presented in Tables 3 and 4.

Table 3: Pharmacokinetic parameters of ELOCTA using the one-stage clotting assay

Pharmacokinetic parameters ¹	ELOCTA (95% CI)
	N=28
Incremental Recovery (IU/dL per IU/kg)	2.24 (2.11-2.38)
AUC/Dose (IU*h/dL per IU/kg)	51.2 (45.0-58.4)
C _{max} (IU/dL)	108 (101-115)
CL (mL/h/kg)	1.95 (1.71-2.22)
t _{1/2} (h)	19.0 (17.0-21.1)
MRT (h)	25.2 (22.7-27.9)
V _{ss} (mL/kg)	49.1 (46.6-51.7)

¹ Pharmacokinetic parameters are presented in Geometric Mean (95% CI)
Abbreviations: CI = confidence interval; C_{max} = maximum activity; AUC = area under the FVIII activity time curve; t_{1/2} = terminal half-life; CL = clearance; V_{ss} = volume of distribution at steady-state; MRT = mean residence time.

Table 4: Pharmacokinetic parameters of ELOCTA using the chromogenic assay

Pharmacokinetic parameters ¹	ELOCTA (95% CI)
	N=27
Incremental Recovery (IU/dL per IU/kg)	2.49 (2.28-2.73)
AUC/Dose (IU*h/dL per IU/kg)	47.5 (41.6-54.2)
C _{max} (IU/dL)	131 (104-165)
CL (mL/h/kg)	2.11 (1.85-2.41)
t _{1/2} (h)	20.9 (18.2-23.9)
MRT (h)	25.0 (22.4-27.8)
V _{ss} (mL/kg)	52.6 (47.4-58.3)

¹ Pharmacokinetic parameters are presented in Geometric Mean (95% CI)
Abbreviations: CI = confidence interval; C_{max} = maximum activity; AUC = area under the FVIII activity time curve; t_{1/2} = terminal half-life; CL = clearance; V_{ss} = volume of distribution at steady-state; MRT = mean residence time.

The PK data demonstrate that ELOCTA has a prolonged circulating half-life.

Paediatric population

Pharmacokinetic parameters of ELOCTA were determined for adolescents in study I (pharmacokinetic sampling was conducted pre-dose followed by assessment at multiple time points up to 120 hours (5 days) post-dose) and for children in study II (pharmacokinetic sampling was conducted pre-dose followed by assessment at multiple time points up to 72 hours (3 days) post-dose). Tables 5 and 6 present the pharmacokinetic parameters calculated from the paediatric data of subjects less than 18 years of age.

Table 5: Pharmacokinetic parameters of ELOCTA for paediatrics using the one-stage clotting assay

Pharmacokinetic parameters ¹	Study II		Study I*
	<6 years	6 to <12 years	12 to <18 years
	N = 23	N = 31	N = 11
Incremental Recovery (IU/dL per IU/kg)	1.90 (1.79-2.02)	2.30 (2.04-2.59)	1.81 (1.56-2.09)
AUC/Dose (IU*h/dL per IU/kg)	28.9 (25.6-32.7)	38.4 (33.2-44.4)	38.2 (34.0-42.9)
t _{1/2} (h)	12.3 (11.0-13.7)	13.5 (11.4-15.8)	16.0 (13.9-18.5)
MRT (h)	16.8 (15.1-18.6)	19.0 (16.2-22.3)	22.7 (19.7-26.1)
CL (mL/h/kg)	3.46 (3.06-3.91)	2.61 (2.26-3.01)	2.62 (2.33-2.95)
V _{ss} (mL/kg)	57.9 (54.1-62.0)	49.5 (44.1-55.6)	59.4 (52.7-67.0)

¹ Pharmacokinetic parameters are presented in Geometric Mean (95% CI)

Abbreviations: CI = confidence interval; AUC = area under the FVIII activity time curve; t_{1/2} = terminal half-life;

CL = clearance; MRT = mean residence time; V_{ss} = volume of distribution at steady-state

*Pharmacokinetic parameters in 12 to <18 years included subjects from all the arms in Study I with different sampling schemes

Table 6: Pharmacokinetic parameters of ELOCTA for paediatrics using the chromogenic assay

Pharmacokinetic parameters ¹	Study II		Study I*
	<6 years	6 to <12 years	12 to <18 years
	N = 24	N = 27	N = 11
Incremental Recovery (IU/dL per IU/kg)	1.88 (1.73-2.05)	2.08 (1.91-2.25)	1.91 (1.61-2.27)
AUC/Dose (IU*h/dL per IU/kg)	25.9 (23.4-28.7)	32.8 (28.2-38.2)	40.8 (29.3-56.7)
t _{1/2} (h)	14.3 (12.6-16.2)	15.9 (13.8-18.2)	17.5 (12.7-24.0)
MRT (h)	17.2 (15.4-19.3)	20.7 (18.0-23.8)	23.5 (17.0-32.4)
CL (mL/h/kg)	3.86 (3.48-4.28)	3.05 (2.62-3.55)	2.45 (1.76-3.41)
V _{ss} (mL/kg)	66.5 (59.8-73.9)	63.1 (56.3-70.9)	57.6 (50.2-65.9)

¹ Pharmacokinetic parameters are presented in Geometric Mean (95% CI)

Abbreviations: CI = confidence interval; AUC = area under the FVIII activity time curve; t_{1/2} = terminal half-life;

CL = clearance; MRT = mean residence time; V_{ss} = volume of distribution at steady-state

* Pharmacokinetic parameters in 12 to <18 years included subjects from all the arms in Study I with different sampling schemes

In comparison with adolescents and adults, children less than 12 years of age may have a higher clearance and a shorter half-life which is consistent with observations of other coagulation factors. These differences should be taken into account when dosing.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on acute and repeated dose toxicity studies (which included assessments of local toxicity and safety pharmacology). Studies to investigate genotoxicity, carcinogenicity, toxicity to reproduction or embryo-foetal development have not been conducted. In a placental transfer study, ELOCTA has been shown to cross the placenta in small amounts in mice.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder

Sucrose

Sodium chloride

Histidine

Calcium chloride dihydrate

Polysorbate 20

Sodium hydroxide (for pH adjustment)

Hydrochloric acid (for pH adjustment)

Solvent

Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

Only the provided infusion set should be used because treatment failure can occur as a consequence of coagulation factor VIII adsorption to the internal surfaces of some injection equipment.

6.3 Shelf life

Unopened vial

5 years

During the shelf-life, the product may be stored at room temperature (up to 30°C) for a single period not exceeding 6 months. The date that the product is removed from refrigeration should be recorded on the carton. After storage at room temperature, the product may not be returned to the refrigerator. Do not use beyond the expiry date printed on the vial or six months after removing the carton from refrigeration, whichever is earlier.

After reconstitution

After reconstitution, chemical and physical stability has been demonstrated for 6 hours when stored at room temperature (up to 30°C). Protect product from direct sunlight. After reconstitution, if the product is not used within 6 hours, it must be discarded. From a microbiological point of view, the product should be used immediately after reconstitution. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C). Do not freeze. Keep the vial in the outer carton in order to protect from light.

For storage conditions after reconstitution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Each pack contains:

- powder in a type 1 glass vial with a chlorobutyl rubber stopper
- 3 mL solvent in a type 1 glass pre-filled syringe with a bromobutyl rubber plunger stopper
- a plunger rod
- a sterile vial adapter for reconstitution
- a sterile infusion set
- two alcohol swabs
- two plasters
- one gauze pad.

Pack size of 1.

6.6 Special precautions for disposal and other handling

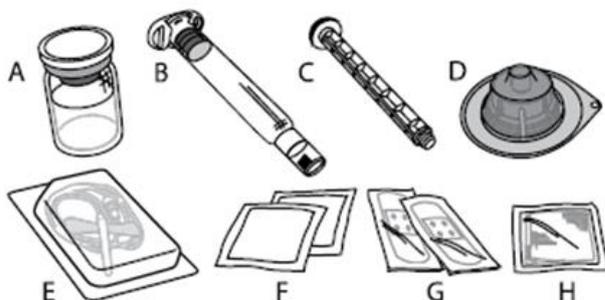
The vial of lyophilised product powder for injection must be reconstituted with the supplied solvent (water for injections) from the pre-filled syringe using the sterile vial adapter for reconstitution.

The vial should be gently swirled until all of the powder is dissolved.

Reconstituted medicinal product should be inspected visually for particulate matter and discoloration prior to administration. The solution should be clear to slightly opalescent and colourless. Do not use solutions that are cloudy or have deposits.

Additional information on reconstitution and administration:

ELOCTA is administered by intravenous (IV) injection after dissolving the powder for injection with the solvent supplied in the pre-filled syringe. ELOCTA pack contains:

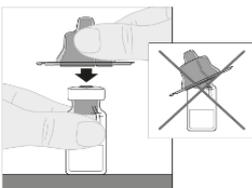


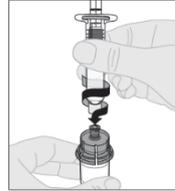
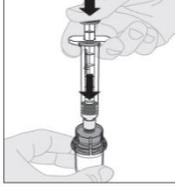
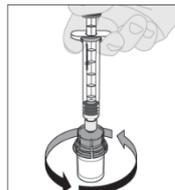
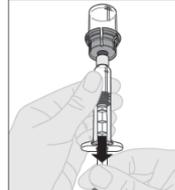
- A) 1 Powder vial
- B) 3 mL solvent in pre-filled syringe
- C) 1 Plunger rod
- D) 1 Vial adapter
- E) 1 Infusion set
- F) 2 Alcohol swabs
- G) 2 Plasters
- H) 1 Gauze pad

ELOCTA should not be mixed with other solutions for injection or infusion.

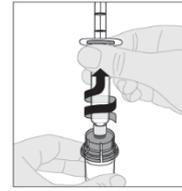
Wash your hands before opening the pack.

Preparation:

1.	Check the name and strength of the package, to make sure it contains the correct medicine. Check the expiry date on the ELOCTA carton. Do not use if the medicine has expired.	
2.	If ELOCTA has been stored in a refrigerator, allow the vial of ELOCTA (A) and the syringe with solvent (B) to reach room temperature before use. Do not use external heat.	
3.	Place the vial on a clean flat surface. Remove the plastic flip-top cap from the ELOCTA vial.	
4.	Wipe the top of the vial with one of the alcohol swabs (F) provided in the pack, and allow to air dry. Do not touch the top of the vial or allow it to touch anything else once wiped.	
5.	Peel back the protective paper lid from the clear plastic vial adapter (D). Do not remove the adapter from its protective cap. Do not touch the inside of the vial adapter package.	
6.	Place the vial on a flat surface. Hold the vial adapter in its protective cap and place it squarely over the top of the vial. Press down firmly until the adapter snaps into place on top of the vial, with the adapter spike penetrating the vial stopper.	

<p>7. Attach the plunger rod (C) to the solvent syringe by inserting the tip of the plunger rod into the opening in the syringe plunger. Turn the plunger rod firmly clockwise until it is securely seated in the syringe plunger.</p>	
<p>8. Break off the white, tamper-resistant, plastic cap from the solvent syringe by bending at the perforation cap until it snaps off. Set the cap aside by placing it with the top down on a flat surface. Do not touch the inside of the cap or the syringe tip.</p>	
<p>9. Lift the protective cap away from the adapter and discard.</p>	
<p>10. Connect the solvent syringe to the vial adapter by inserting the tip of the syringe into the adapter opening. Firmly push and turn the syringe clockwise until it is securely connected.</p>	
<p>11. Slowly depress the plunger rod to inject all the solvent into the ELOCTA vial.</p>	
<p>12. With the syringe still connected to the adapter and the plunger rod pressed down, gently swirl the vial until the powder is dissolved. Do not shake.</p>	
<p>13. The final solution must be inspected visually before administration. The solution should appear clear to slightly opalescent and colourless. Do not use the solution if cloudy or contains visible particles.</p>	
<p>14. Ensuring that the syringe plunger rod is still fully pressed down, invert the vial. Slowly pull on the plunger rod to draw back all the solution through the vial adapter into the syringe.</p>	

15. Detach the syringe from the vial adapter by gently pulling and turning the syringe counterclockwise.



Note: If you use more than one vial of ELOCTA per injection, each vial should be prepared separately as per the previous instructions (steps 1 to 13) and the solvent syringe should be removed, leaving the vial adapter in place. A single large luer lock syringe may be used to draw back the prepared contents of each of the individual vials.

16. Discard the vial and the adapter.

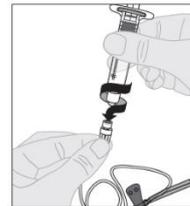
Note: If the solution is not to be used immediately, the syringe cap should be carefully put back on the syringe tip. Do not touch the syringe tip or the inside of the cap.

After preparation, ELOCTA can be stored at room temperature for up to 6 hours before administration. After this time, the prepared ELOCTA should be discarded. Protect from direct sunlight.

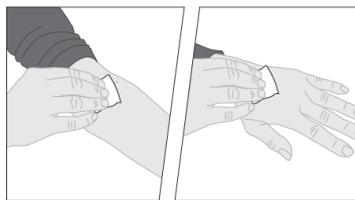
Administration (Intravenous injection):

ELOCTA should be administered using the infusion set (E) provided in this pack.

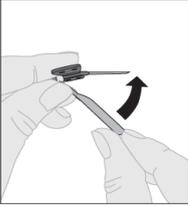
1. Open the infusion set package and remove the cap at the end of the tubing. Attach the syringe with the prepared ELOCTA solution to the end of the infusion set tubing by turning clockwise.



2. If needed apply a tourniquet and prepare the injection site by wiping the skin well with the other alcohol swab provided in the pack.



3. Remove any air in the infusion set tubing by slowly depressing on the plunger rod until liquid has reached the infusion set needle. Do not push the solution through the needle. Remove the clear plastic protective cover from the needle.
4. Insert the infusion set needle into a vein as instructed by your doctor or nurse and remove the tourniquet. If preferred, you may use one of the plasters (G) provided in the pack to hold the plastic wings of the needle in place at the injection site. The prepared product should be injected intravenously over several minutes. Your doctor may change your recommended injection rate to make it more comfortable for you.

<p>5. After completing the injection and removing the needle, you should fold over the needle protector and snap it over the needle.</p>	
<p>6. Please safely dispose of the used needle, any unused solution, the syringe and the empty vial in an appropriate medical waste container as these materials may hurt others if not disposed of properly. Do not reuse equipment.</p>	

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Swedish Orphan Biovitrum AB (publ)
SE-112 76 Stockholm
Sweden

8. MARKETING AUTHORISATION NUMBER(S)

- EU/1/15/1046/001
- EU/1/15/1046/002
- EU/1/15/1046/003
- EU/1/15/1046/004
- EU/1/15/1046/005
- EU/1/15/1046/006
- EU/1/15/1046/007
- EU/1/15/1046/008

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 19 November 2015
Date of latest renewal: 19 August 2020

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency <http://www.ema.europa.eu>.

ANNEX II

- A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**
- C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**
- D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers of the biological active substance

Biogen Inc
250 Binney Street
Cambridge, MA
02142
USA

Biogen Inc.
5000 Davis Drive
Research Triangle Park, NC 27709
USA

Name and address of the manufacturer responsible for batch release

Swedish Orphan Biovitrum AB (publ)
Norra Stationsgatan 93, 113 64
Stockholm
Sweden

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

• **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

• **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

ELOCTA 250 IU powder and solvent for solution for injection

efmoroctocog alfa
(recombinant coagulation factor VIII, Fc fusion protein)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 powder vial contains 250 IU efmoroctocog alfa (approx. 83 IU/mL after reconstitution)

3. LIST OF EXCIPIENTS

Powder: sucrose, sodium chloride, histidine, calcium chloride dihydrate, polysorbate 20, sodium hydroxide, hydrochloric acid.

Solvent: water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for solution for injection

Content: 1 powder vial, 3 mL solvent in pre-filled syringe, 1 plunger rod, 1 vial adapter, 1 infusion set, 2 alcohol swabs, 2 plasters, 1 gauze.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intravenous use, after reconstitution.
Read the package leaflet before use.

An instructional video on how to prepare and administer ELOCTA is available by scanning the QR code with a smartphone or via the website.

QR code to be included+ <http://www.elocta-instructions.com>

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

Use within 6 hours after reconstitution.

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.

Do not freeze.

Keep the vial in the outer carton in order to protect from light.

Can be stored at room temperature (up to 30°C) for a single period up to 6 months. Must not be returned to refrigerator after storage at room temperature. Date removed from refrigerator:

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Swedish Orphan Biovitrum AB (publ)

SE-112 76 Stockholm

Sweden

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1046/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

ELOCTA 250

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

ELOCTA 250 IU powder for injection

efmoroctocog alfa
recombinant coagulation factor VIII
IV

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

250 IU

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

ELOCTA 500 IU powder and solvent for solution for injection

efmoroctocog alfa
(recombinant coagulation factor VIII, Fc fusion protein)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 powder vial contains 500 IU efmorococog alfa (approx. 167 IU/mL after reconstitution)

3. LIST OF EXCIPIENTS

Powder: sucrose, sodium chloride, histidine, calcium chloride dihydrate, polysorbate 20, sodium hydroxide, hydrochloric acid.

Solvent: water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for solution for injection

Content: 1 powder vial, 3 mL solvent in pre-filled syringe, 1 plunger rod, 1 vial adapter, 1 infusion set, 2 alcohol swabs, 2 plasters, 1 gauze.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intravenous use, after reconstitution.
Read the package leaflet before use.

An instructional video on how to prepare and administer ELOCTA is available by scanning the QR code with a smartphone or via the website.

QR code to be included+ <http://www.elocta-instructions.com>

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

Use within 6 hours after reconstitution.

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.

Do not freeze.

Keep the vial in the outer carton in order to protect from light.

Can be stored at room temperature (up to 30°C) for a single period up to 6 months. Must not be returned to refrigerator after storage at room temperature. Date removed from refrigerator:

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Swedish Orphan Biovitrum AB (publ)

SE-112 76 Stockholm

Sweden

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1046/002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

ELOCTA 500

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

ELOCTA 500 IU powder for injection

efmoroctocog alfa
recombinant coagulation factor VIII
IV

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

500 IU

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

ELOCTA 750 IU powder and solvent for solution for injection

efmoroctocog alfa
(recombinant coagulation factor VIII, Fc fusion protein)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 powder vial contains 750 IU efmoroctocog alfa (approx. 250 IU/mL after reconstitution)

3. LIST OF EXCIPIENTS

Powder: sucrose, sodium chloride, histidine, calcium chloride dihydrate, polysorbate 20, sodium hydroxide, hydrochloric acid.

Solvent: water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for solution for injection

Content: 1 powder vial, 3 mL solvent in pre-filled syringe, 1 plunger rod, 1 vial adapter, 1 infusion set, 2 alcohol swabs, 2 plasters, 1 gauze.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intravenous use, after reconstitution.
Read the package leaflet before use.

An instructional video on how to prepare and administer ELOCTA is available by scanning the QR code with a smartphone or via the website.

QR code to be included+ <http://www.elocta-instructions.com>

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

Use within 6 hours after reconstitution.

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.

Do not freeze.

Keep the vial in the outer carton in order to protect from light.

Can be stored at room temperature (up to 30°C) for a single period up to 6 months. Must not be returned to refrigerator after storage at room temperature. Date removed from refrigerator:

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Swedish Orphan Biovitrum AB (publ)

SE-112 76 Stockholm

Sweden

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1046/003

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

ELOCTA 750

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

ELOCTA 750 IU powder for injection

efmoroctocog alfa
recombinant coagulation factor VIII
IV

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

750 IU

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

ELOCTA 1000 IU powder and solvent for solution for injection

efmoroctocog alfa
(recombinant coagulation factor VIII, Fc fusion protein)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 powder vial contains 1000 IU efmoroctocog alfa (approx. 333 IU/mL after reconstitution)

3. LIST OF EXCIPIENTS

Powder: sucrose, sodium chloride, histidine, calcium chloride dihydrate, polysorbate 20, sodium hydroxide, hydrochloric acid.

Solvent: water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for solution for injection

Content: 1 powder vial, 3 mL solvent in pre-filled syringe, 1 plunger rod, 1 vial adapter, 1 infusion set, 2 alcohol swabs, 2 plasters, 1 gauze.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intravenous use, after reconstitution.
Read the package leaflet before use.

An instructional video on how to prepare and administer ELOCTA is available by scanning the QR code with a smartphone or via the website.

QR code to be included+ <http://www.elocta-instructions.com>

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

Use within 6 hours after reconstitution.

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.

Do not freeze.

Keep the vial in the outer carton in order to protect from light.

Can be stored at room temperature (up to 30°C) for a single period up to 6 months. Must not be returned to refrigerator after storage at room temperature. Date removed from refrigerator:

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Swedish Orphan Biovitrum AB (publ)

SE-112 76 Stockholm

Sweden

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1046/004

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

ELOCTA 1000

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

ELOCTA 1000 IU powder for injection

efmoroctocog alfa
recombinant coagulation factor VIII
IV

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1000 IU

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

ELOCTA 1500 IU powder and solvent for solution for injection

efmoroctocog alfa
(recombinant coagulation factor VIII, Fc fusion protein)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 powder vial contains 1500 IU efmoroctocog alfa (approx. 500 IU/mL after reconstitution)

3. LIST OF EXCIPIENTS

Powder: sucrose, sodium chloride, histidine, calcium chloride dihydrate, polysorbate 20, sodium hydroxide, hydrochloric acid.

Solvent: water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for solution for injection

Content: 1 powder vial, 3 mL solvent in pre-filled syringe, 1 plunger rod, 1 vial adapter, 1 infusion set, 2 alcohol swabs, 2 plasters, 1 gauze.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intravenous use, after reconstitution.
Read the package leaflet before use.

An instructional video on how to prepare and administer ELOCTA is available by scanning the QR code with a smartphone or via the website.

QR code to be included+ <http://www.elocta-instructions.com>

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

Use within 6 hours after reconstitution.

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.

Do not freeze.

Keep the vial in the outer carton in order to protect from light.

Can be stored at room temperature (up to 30°C) for a single period up to 6 months. Must not be returned to refrigerator after storage at room temperature. Date removed from refrigerator:

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Swedish Orphan Biovitrum AB (publ)

SE-112 76 Stockholm

Sweden

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1046/005

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

ELOCTA 1500

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

ELOCTA 1500 IU powder for injection

efmoroctocog alfa
recombinant coagulation factor VIII
IV

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1500 IU

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

ELOCTA 2000 IU powder and solvent for solution for injection

efmoroctocog alfa
(recombinant coagulation factor VIII, Fc fusion protein)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 powder vial contains 2000 IU efmoroctocog alfa (approx. 667 IU/mL after reconstitution)

3. LIST OF EXCIPIENTS

Powder: sucrose, sodium chloride, histidine, calcium chloride dihydrate, polysorbate 20, sodium hydroxide, hydrochloric acid.

Solvent: water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for solution for injection

Content: 1 powder vial, 3 mL solvent in pre-filled syringe, 1 plunger rod, 1 vial adapter, 1 infusion set, 2 alcohol swabs, 2 plasters, 1 gauze.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intravenous use, after reconstitution.
Read the package leaflet before use.

An instructional video on how to prepare and administer ELOCTA is available by scanning the QR code with a smartphone or via the website.

QR code to be included+ <http://www.elocta-instructions.com>

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

Use within 6 hours after reconstitution.

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.

Do not freeze.

Keep the vial in the outer carton in order to protect from light.

Can be stored at room temperature (up to 30°C) for a single period up to 6 months. Must not be returned to refrigerator after storage at room temperature. Date removed from refrigerator:

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Swedish Orphan Biovitrum AB (publ)

SE-112 76 Stockholm

Sweden

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1046/006

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

ELOCTA 2000

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

ELOCTA 2000 IU powder for injection

efmoroctocog alfa
recombinant coagulation factor VIII
IV

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

2000 IU

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

ELOCTA 3000 IU powder and solvent for solution for injection

efmoroctocog alfa
(recombinant coagulation factor VIII, Fc fusion protein)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 powder vial contains 3000 IU efmoroctocog alfa (approx. 1000 IU/mL after reconstitution)

3. LIST OF EXCIPIENTS

Powder: sucrose, sodium chloride, histidine, calcium chloride dihydrate, polysorbate 20, sodium hydroxide, hydrochloric acid.

Solvent: water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for solution for injection

Content: 1 powder vial, 3 mL solvent in pre-filled syringe, 1 plunger rod, 1 vial adapter, 1 infusion set, 2 alcohol swabs, 2 plasters, 1 gauze.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intravenous use, after reconstitution.
Read the package leaflet before use.

An instructional video on how to prepare and administer ELOCTA is available by scanning the QR code with a smartphone or via the website.

QR code to be included+ <http://www.elocta-instructions.com>

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

Use within 6 hours after reconstitution.

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.

Do not freeze.

Keep the vial in the outer carton in order to protect from light.

Can be stored at room temperature (up to 30°C) for a single period up to 6 months. Must not be returned to refrigerator after storage at room temperature. Date removed from refrigerator:

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Swedish Orphan Biovitrum AB (publ)

SE-112 76 Stockholm

Sweden

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1046/007

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

ELOCTA 3000

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

ELOCTA 3000 IU powder for injection

efmoroctocog alfa
recombinant coagulation factor VIII
IV

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3000 IU

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

ELOCTA 4000 IU powder and solvent for solution for injection

efmoroctocog alfa
(recombinant coagulation factor VIII, Fc fusion protein)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 powder vial contains 4000 IU efmoroctocog alfa (approx. 1333 IU/mL after reconstitution)

3. LIST OF EXCIPIENTS

Powder: sucrose, sodium chloride, histidine, calcium chloride dihydrate, polysorbate 20, sodium hydroxide, hydrochloric acid.

Solvent: water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for solution for injection

Content: 1 powder vial, 3 mL solvent in pre-filled syringe, 1 plunger rod, 1 vial adapter, 1 infusion set, 2 alcohol swabs, 2 plasters, 1 gauze.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intravenous use, after reconstitution.
Read the package leaflet before use.

An instructional video on how to prepare and administer ELOCTA is available by scanning the QR code with a smartphone or via the website.

QR code to be included+ <http://www.elocta-instructions.com>

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

Use within 6 hours after reconstitution.

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.

Do not freeze.

Keep the vial in the outer carton in order to protect from light.

Can be stored at room temperature (up to 30°C) for a single period up to 6 months. Must not be returned to refrigerator after storage at room temperature. Date removed from refrigerator:

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Swedish Orphan Biovitrum AB (publ)

SE-112 76 Stockholm

Sweden

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1046/008

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

ELOCTA 4000

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

ELOCTA 4000 IU powder for injection

efmoroctocog alfa
recombinant coagulation factor VIII
IV

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

4000 IU

6. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS
PRE-FILLED SYRINGE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Solvent for ELOCTA
water for injections

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 mL

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: information for the user

ELOCTA 250 IU powder and solvent for solution for injection
ELOCTA 500 IU powder and solvent for solution for injection
ELOCTA 750 IU powder and solvent for solution for injection
ELOCTA 1000 IU powder and solvent for solution for injection
ELOCTA 1500 IU powder and solvent for solution for injection
ELOCTA 2000 IU powder and solvent for solution for injection
ELOCTA 3000 IU powder and solvent for solution for injection
ELOCTA 4000 IU powder and solvent for solution for injection

efmoroctocog alfa (recombinant coagulation factor VIII)

Read all of this leaflet carefully before you start using this medicine because it contains important information for you

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What ELOCTA is and what it is used for
2. What you need to know before you use ELOCTA
3. How to use ELOCTA
4. Possible side effects
5. How to store ELOCTA
6. Contents of the pack and other information

1. What ELOCTA is and what it is used for

ELOCTA contains the active substance efmoroctocog alfa, a recombinant coagulation factor VIII, Fc fusion protein. Factor VIII is a protein produced naturally in the body and is necessary for the blood to form clots and stop bleeding.

ELOCTA is a medicine used for the treatment and prevention of bleeding in all age groups of patients with haemophilia A (inherited bleeding disorder caused by factor VIII deficiency).

ELOCTA is prepared by recombinant technology without addition of any human- or animal-derived components in the manufacturing process.

How ELOCTA works

In patients with haemophilia A, factor VIII is missing or not working properly. ELOCTA is used to replace the missing or deficient factor VIII. ELOCTA increases factor VIII level in the blood and temporarily corrects the bleeding tendency.

2. What you need to know before you use ELOCTA

Do not use ELOCTA:

- if you are allergic to efmoctocog alfa or any other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using ELOCTA.

- There is a small chance that you may experience an anaphylactic reaction (a severe, sudden allergic reaction) to ELOCTA. Signs of allergic reactions may include generalised itching, hives, tightness of the chest, difficulty breathing and low blood pressure. If any of these symptoms occur, stop the injection immediately and contact your doctor.
- The formation of inhibitors (antibodies) is a known complication that can occur during treatment with all factor VIII medicines. These inhibitors, especially at high levels, stop the treatment working properly and you or your child will be monitored carefully for the development of these inhibitors. If your or your child's bleeding is not being controlled with ELOCTA, tell your doctor immediately.

Cardiovascular events

If you have heart disease or are at risk for heart disease, take special care when using factor VIII medicines and talk to your doctor.

Catheter-related complications

If you require a central venous access device (CVAD), risk of CVAD-related complications including local infections, presence of bacteria in the blood and catheter site thrombosis should be considered.

Documentation

It is strongly recommended that every time ELOCTA is given, the name and batch number of the product are recorded.

Other medicines and ELOCTA

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines

No effects on ability to drive or use of machines have been observed.

ELOCTA contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium-free'. However, depending on your body weight and dose, you could receive more than one vial. This should be taken into consideration if you are on a controlled sodium diet.

ELOCTA contains polysorbate

This medicine contains 0.4 mg of polysorbate 20 in each vial. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

3. How to use ELOCTA

Treatment with ELOCTA will be started by a doctor who is experienced in the care of patients with haemophilia. Always use this medicine exactly as your doctor has told you (see Instructions for preparation and administration). Check with your doctor, pharmacist or nurse if you are not sure.

ELOCTA is given as an injection into a vein. Your doctor will calculate the dose of ELOCTA (in International Units or "IU") depending on your individual needs for factor VIII replacement therapy and on

whether it is used for prevention or treatment of bleeding. Talk to your doctor if you think that your bleeding is not being controlled with the dose you receive.

How often you need an injection will depend on how well ELOCTA is working for you. Your doctor will perform appropriate laboratory tests to make sure that you have adequate factor VIII levels in your blood.

Treatment of bleeding

The dose of ELOCTA is calculated depending on your body weight and the factor VIII levels to be achieved. The target factor VIII levels will depend on the severity and location of the bleeding.

Prevention of bleeding

The usual dose of ELOCTA is 50 IU per kg of body weight, given every 3 to 5 days. The dose may be adjusted by your doctor in the range of 25 to 65 IU per kg of body weight. In some cases, especially in younger patients, shorter dosing intervals or higher doses may be necessary.

Use in children and adolescents

ELOCTA can be used in children and adolescents of all ages. In children below the age of 12, higher doses or more frequent injections may be needed.

If you use more ELOCTA than you should

Tell your doctor as soon as possible. You should always use ELOCTA exactly as your doctor has told you, check with your doctor, pharmacist or nurse if you are not sure.

If you forget to use ELOCTA

Do not take a double dose to make up for a forgotten dose. Take your dose as soon as you remember and then resume your normal dosing schedule. If you are not sure what to do, ask your doctor or pharmacist.

If you stop using ELOCTA

Do not stop using ELOCTA without consulting your doctor. If you stop using ELOCTA you may no longer be protected against bleeding or a current bleed may not stop.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If severe, sudden allergic reactions (anaphylactic reaction) occur, the injection must be stopped immediately. You must contact your doctor immediately if you experience any of the following symptoms of allergic reactions: swelling of the face, rash, generalised itching, hives, tightness of the chest, difficulty breathing, burning and stinging at the injection site, chills, flushing, headache, low blood pressure, general feeling of being unwell, nausea, restlessness and fast heartbeat, feeling dizzy or loss of consciousness.

For children previously untreated with factor VIII medicines, inhibitor antibodies (see section 2) may form very commonly (more than 1 in 10 patients); however, patients who have received previous treatment with factor VIII (more than 150 days of treatment) the risk is uncommon (less than 1 in 100 patients). If this happens the medicines may stop working properly and you may experience persistent bleeding. If this happens, you should contact your doctor immediately.

The following side effects may occur with this medicine.

Uncommon side effects (may affect up to 1 in 100 people)

Headache, dizziness, taste alteration, slow heartbeat, high blood pressure, hot flushes, vascular pain after injection, cough, lower abdominal pain, rash, papular rash, device-related thrombosis, joint swelling, muscle pain, back pain, joint pain, general discomfort, chest pain, feeling cold, feeling hot and low blood pressure.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in [Appendix V](#). By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store ELOCTA

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and the vial label after “EXP”. The expiry date refers to the last day of that month. Do not use this medicine if it has been stored at room temperature for longer than 6 months.

Store in a refrigerator (2°C - 8°C).

Do not freeze.

Store in the original package in order to protect from light.

Alternatively, ELOCTA may be stored at room temperature (up to 30°C) for a single period not exceeding 6 months. Record on the carton the date that ELOCTA is removed from the refrigerator and set at room temperature. After storage at room temperature, the product must not be put back in the refrigerator.

Once you have prepared ELOCTA it should be used right away. If you cannot use the prepared ELOCTA solution immediately, it should be used within 6 hours. Do not refrigerate the prepared solution. Protect the prepared solution from direct sunlight.

The prepared solution will be clear to slightly opalescent and colourless. Do not use this medicine if you notice that it is cloudy or contains visible particles.

Discard any unused solution appropriately. Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What ELOCTA contains

- The active substance is efmoctocog alfa (recombinant coagulation factor VIII, Fc fusion protein). Each vial of ELOCTA contains nominally 250, 500, 750, 1000, 1500, 2000, 3000 or 4000 IU efmoctocog alfa.
- The other ingredients are sucrose, sodium chloride, histidine, calcium chloride dihydrate, polysorbate 20, sodium hydroxide, hydrochloric acid and water for injections. If you are on a controlled sodium diet, see section 2.

What ELOCTA looks like and contents of the pack

ELOCTA is provided as a powder and solvent for solution for injection. The powder is a white to off-white powder or cake. The solvent provided for preparation of the solution to inject, is a clear, colourless solution. After preparation, the solution to inject is clear to slightly opalescent and colourless.

Each pack of ELOCTA contains 1 powder vial, 3 mL solvent in pre-filled syringe, 1 plunger rod, 1 vial adapter, 1 infusion set, 2 alcohol swabs, 2 plasters and 1 gauze pad.

Marketing Authorisation Holder

Swedish Orphan Biovitrum AB (publ)
SE-112 76 Stockholm
Sweden
Phone: +46 8 697 20 00

Manufacturer

Swedish Orphan Biovitrum AB (publ)
Norra Stationsgatan 93
SE-113 64 Stockholm
Sweden

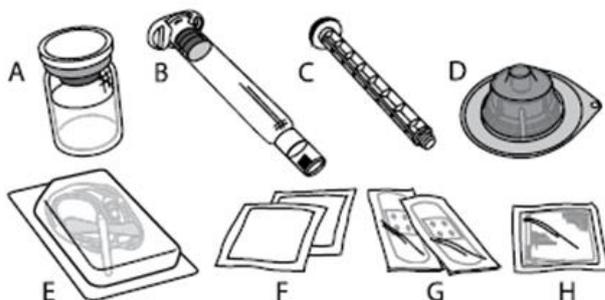
This leaflet was last revised in

Detailed information on this medicine is available on the European Medicines Agency web site:
<http://www.ema.europa.eu>

Turn the leaflet over for instructions for preparation and administration

Instructions for preparation and administration

ELOCTA is administered by intravenous (IV) injection after dissolving the powder for injection with the solvent supplied in the pre-filled syringe. ELOCTA pack contains:



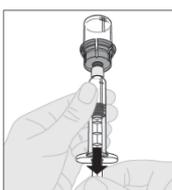
- A) 1 Powder vial
- B) 3 mL solvent in pre-filled syringe
- C) 1 Plunger rod
- D) 1 Vial adapter
- E) 1 Infusion set
- F) 2 Alcohol swabs
- G) 2 Plasters
- H) 1 Gauze pad

ELOCTA should not be mixed with other solutions for injection or infusion.

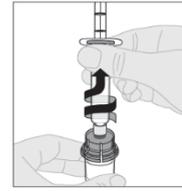
Wash your hands before opening the pack.

Preparation:

1. Check the name and strength of the package, to make sure it contains the correct medicine. Check the expiry date on the ELOCTA carton. Do not use if the medicine has expired.	
2. If ELOCTA has been stored in a refrigerator, allow the vial of ELOCTA (A) and the syringe with solvent (B) to reach room temperature before use. Do not use external heat.	
3. Place the vial on a clean flat surface. Remove the plastic flip-top cap from the ELOCTA vial.	
4. Wipe the top of the vial with one of the alcohol swabs (F) provided in the pack, and allow to air dry. Do not touch the top of the vial or allow it to touch anything else once wiped.	
5. Peel back the protective paper lid from the clear plastic vial adapter (D). Do not remove the adapter from its protective cap. Do not touch the inside of the vial adapter package.	
6. Place the vial on a flat surface. Hold the vial adapter in its protective cap and place it squarely over the top of the vial. Press down firmly until the adapter snaps into place on top of the vial, with the adapter spike penetrating the vial stopper.	

<p>7. Attach the plunger rod (C) to the solvent syringe by inserting the tip of the plunger rod into the opening in the syringe plunger. Turn the plunger rod firmly clockwise until it is securely seated in the syringe plunger.</p>	
<p>8. Break off the white, tamper-resistant, plastic cap from the solvent syringe by bending at the perforation cap until it snaps off. Set the cap aside by placing it with the top down on a flat surface. Do not touch the inside of the cap or the syringe tip.</p>	
<p>9. Lift the protective cap away from the adapter and discard.</p>	
<p>10. Connect the solvent syringe to the vial adapter by inserting the tip of the syringe into the adapter opening. Firmly push and turn the syringe clockwise until it is securely connected.</p>	
<p>11. Slowly depress the plunger rod to inject all the solvent into the ELOCTA vial.</p>	
<p>12. With the syringe still connected to the adapter and the plunger rod pressed down, gently swirl the vial until the powder is dissolved. Do not shake.</p>	
<p>13. The final solution must be inspected visually before administration. The solution should appear clear to slightly opalescent and colourless. Do not use the solution if cloudy or contains visible particles.</p>	
<p>14. Ensuring that the syringe plunger rod is still fully pressed down, invert the vial. Slowly pull on the plunger rod to draw back all the solution through the vial adapter into the syringe.</p>	

15. Detach the syringe from the vial adapter by gently pulling and turning the syringe counterclockwise.



Note: If you use more than one vial of ELOCTA per injection, each vial should be prepared separately as per the previous instructions (steps 1 to 13) and the solvent syringe should be removed, leaving the vial adapter in place. A single large luer lock syringe may be used to draw back the prepared contents of each of the individual vials.

16. Discard the vial and the adapter.

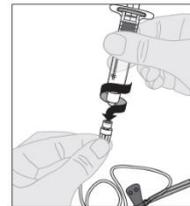
Note: If the solution is not to be used immediately, the syringe cap should be carefully put back on the syringe tip. Do not touch the syringe tip or the inside of the cap.

After preparation, ELOCTA can be stored at room temperature for up to 6 hours before administration. After this time, the prepared ELOCTA should be discarded. Protect from direct sunlight.

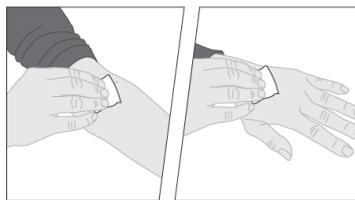
Administration (Intravenous injection):

ELOCTA should be administered using the infusion set (E) provided in this pack.

1. Open the infusion set package and remove the cap at the end of the tubing. Attach the syringe with the prepared ELOCTA solution to the end of the infusion set tubing by turning clockwise.



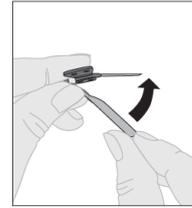
2. If needed apply a tourniquet and prepare the injection site by wiping the skin well with the other alcohol swab provided in the pack.



3. Remove any air in the infusion set tubing by slowly depressing on the plunger rod until liquid has reached the infusion set needle. Do not push the solution through the needle. Remove the clear plastic protective cover from the needle.

4. Insert the infusion set needle into a vein as instructed by your doctor or nurse and remove the tourniquet. If preferred, you may use one of the plasters (G) provided in the pack to hold the plastic wings of the needle in place at the injection site. The prepared product should be injected intravenously over several minutes. Your doctor may change your recommended injection rate to make it more comfortable for you.

5. After completing the injection and removing the needle, you should fold over the needle protector and snap it over the needle.



6. Please safely dispose of the used needle, any unused solution, the syringe and the empty vial in an appropriate medical waste container as these materials may hurt others if not disposed of properly. Do not reuse equipment.