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**BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION**

# **ELOCTA** (efmoroctocog alfa), factor VIII

**No clinical benefit demonstrated by comparison with other coagulation factor VIII products in the treatment and prophylaxis of bleeding in patients with haemophilia A**

## Main points

- ELOCTA has Marketing Authorisation in the treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency). It is indicated in all age groups.
- It is a recombinant FVIII with an extended half-life
- In the absence of direct comparison, the studies do not allow a conclusion about its possible benefit compared with other available FVIIIs in reducing bleeding or frequency of injections, especially in young children.

## Therapeutic use

- The aim of therapeutic management in haemophilia A is the early prevention and control of bleeding and its short- and long-term complications.
- The first-line treatment for haemophilia A is replacement therapy involving the administration of coagulation factor VIII concentrates. It may be administered:
  - in the prevention of bleeding: as primary prophylaxis in children with severe haemophilia aged under 2 years and before the occurrence of a second haemarthrosis, as secondary prophylaxis (long-term or intermittent) after the occurrence of a second haemarthrosis, or during surgery or invasive procedures (depending on the severity and the risk of bleeding expected),
  - as curative treatment ("on demand" treatment) when bleeding occurs that cannot be controlled by local haemostatic measures or is not suitable for treatment with desmopressin or tranexamic acid.
- In children with severe haemophilia, prophylactic treatment is the reference treatment, the main disadvantage of which is its therapeutic weight.
- **Role of the medicinal product in the therapeutic strategy**

  ELOCTA is one of the first-line factor VIII concentrates used in the prophylaxis and treatment of bleeding in haemophilia A.

## Clinical data

- The efficacy and safety of ELOCTA have been evaluated in patients with a severe form of haemophilia A, aged between 1 and 65 years, all previously treated with a factor VIII product and without a history of inhibitors. They have not been compared with those of another factor VIII product. The haemostatic efficacy of ELOCTA has been evaluated in prophylaxis (long-term and in a surgical situation) as well as in on-demand therapy in two phase III studies. In the study carried out in 165 patients aged 12 to 65 years:
  - Depending on the treatment arm, patients received long-term individualised prophylaxis (initially 25 IU/kg on day D1 and 50 IU/kg on day D4 (i.e. twice weekly) and then the doses were adjusted according to the pharmacokinetic and clinical data between 25 and 65 IU/kg every 3 to 5 days) or weekly (65 IU/kg once weekly), or they were treated only on demand during bleeding episodes (10 to 50 IU/kg per injection);
  - The mean annualised bleeding rate was lower in patients receiving individualised prophylactic treatment compared with those only treated on-demand: 2.91 versus 37.25 ($p<0.001$);
  - Under individualised prophylaxis, the median interval between two injections was 3.51 days (2.9 to 5.0);

- 97.8% of bleeding episodes during the study that required administration of ELOCTA were controlled by two injections and a median total dose of 28.23 IU/kg;
- The prophylactic efficacy of ELOCTA in surgery was considered excellent for eight procedures or good for one procedure in all major surgeries performed (n=9);
- The efficacy of the prophylactic regimen as a single weekly injection appeared to be lower than that of the individualised prophylaxis, so this regimen has not been approved by the Marketing Authorisation.

- In the study carried out in children under 12 years of age (71 children aged 1 to 11 years):
  - Everyone received a long-term prophylactic treatment started at a dose of 25 IU/kg on day D1 and 50 IU/kg on D4 (i.e. twice weekly), which could then be adjusted according to the pharmacokinetic and clinical data (maximum dose of 80 IU/kg every 2 days);
  - The mean annualised bleeding rate was 1.96 in the entire population: 0.00 (IQR [0.0; 3.96]) for children under 6 years of age and 2.01 (IQR [0.0; 4.04]) for children between 6 and 11 years;
  - About 53% reported at least one bleeding episode requiring administration of ELOCTA. The majority of bleeding (93%) was controlled by one or two injections of ELOCTA and a total median dose of 54.90 IU/kg;
  - In the absence of major surgery being performed, the efficacy in surgical prophylaxis in children could not be assessed.
- The safety profile is comparable in children and adults. No severe allergic reaction or anaphylactic reaction, or serious thromboembolic event, has been reported. A case of occurrence of transient inhibitors, not confirmed by subsequent tests, was reported in an adult during the clinical trials.
- Conclusion on the clinical trials:
  - The treatment regimens used in the clinical trials for prophylaxis differ from those usually recommended and practised in France: higher injection doses than those usually prescribed, increasing doses rather than decreasing time between injections in case of insufficient efficacy, lack of defined increments, etc.
  - In the absence of direct comparison, these studies do not allow a conclusion about any possible benefit of ELOCTA, compared with other available FVIIIs, in reducing bleeding or frequency of injections, especially in young children.
  - The injected doses of ELOCTA recommended in the SmPC are higher than those recommended for the other available FVIIIs, which could increase the thromboembolic risk (peak activity rate > 150 IU/dL after an injection of 65 IU/kg), especially in those over 65 years of age, not represented in the studies.

## Special prescribing conditions

- Initial 6-month hospital prescription.

## Benefit of the medicinal product

- The actual benefit* of ELOCTA is substantial.
- ELOCTA does not provide clinical added value** (CAV V, non-existent) compared with the other coagulation factor VIII products available.
- Recommends inclusion on the list of reimbursable products for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 17 February 2016 (CT-14817) and is available at **www.has-sante.fr**

* The actual benefit (AB) of a proprietary medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the AB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

** The clinical added value (CAV) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV means "no clinical added value".