INESSS
LE SAVOIR PREND FORME

OCTOBER 2019

Esperoct[MC] (turoctocog alfa pegol) – Hemophilia A

English summary

Une production de l'Institut national d'excellence en santé et en services sociaux (INESSS)

Direction des services de santé et de l'évaluation des technologies

Québec

Le présent rapport a été présenté au Groupe d'experts sur les produits du système du sang de l'Institut national d'excellence en santé et en services sociaux (INESSS) lors de sa réunion du 10 juin 2019 ainsi qu'au Comité scientifique permanent de l'évaluation des médicaments aux fins d'inscription (CSÉMI) de l'INESSS lors de sa réunion du 25 juillet 2019.

Le contenu de cette publication a été rédigé et édité par l'INESSS.

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SUMMARY

Esperoct™ (turoctocog alfa pegol) – Hemophilia A

Mandate

The *Institut national d'excellence en santé et en services sociaux* (INESSS) evaluated the stable blood product Esperoct™ (turoctocog alfa pegol, N8-GP), a recombinant factor VIII (FVIII) conjugated with a polyethylene glycol (PEG) molecule and administered by intravenous injection. It is indicated for routine prophylaxis, on-demand treatment and the management of perioperative bleeding in patients with hemophilia A (congenital FVIII deficiency).

The recombinant FVIII Advate™, Adynovate™, Eloctate™, Kovaltry™, Nuwiq™, Xyntha™ (including Xyntha Solofuse™) and Zonovate™ are currently listed on the *Liste des produits du système du sang du Québec*. Nuwiq™ and Zonovate™ are distributed by Héma-Québec, and Eloctate™ is available under an MSSS directive.

Evaluation process

Published trials and manufacturer data were reviewed to document the efficacy, safety and efficiency of Esperoct™. Experiential and contextual data from consultations with experts are presented as well.

Health needs

Hemophilia A is the most common congenital blood disorder. It is caused by a deficiency in hemostatic factor VIII (FVIII). Since hemophilia A is an X-linked recessive disease, most individuals affected are males. The diagnosis is made around the second year of life, and it is estimated that about one in 5,000 male newborns will develop the disease. The prevalence among males ranges from 7,000 to 18,000 cases, depending on the country.

FVIII deficiency causes longer-than-normal clotting times. In severe cases, it leads to frequent spontaneous (non-traumatic) bleeding episodes in the joints (hemarthrosis) and soft tissues. FVIII prophylaxis, either plasma-derived or in recombinant form, is the preferred treatment. The prophylactic treatment consists of several weekly or even daily intravenous injections to replace the missing FVIII. Some individuals with a low bleeding rate are treated only when bleeding occurs.

Despite an overall good management of hemophilia A in Québec that significantly reduces the number of spontaneous bleeds, FVIII prophylaxis represents a considerable burden for the patients and their family. This situation can be even more challenging for caregivers of young school or preschool children. Additional therapeutic options that would further reduce the number of bleeds and simplify product administration and reduce dose frequency would remedy the shortcomings of the current treatments.

Efficacy

- For individuals over 12 years of age treated prophylactically with Esperoct™, the estimated median annualized bleeding rate was 1.18, a 96% reduction compared to patients treated on-demand (Pathfinder™ 2 study). Over the mean study duration of 299 days, 40% of the individuals treated prophylactically reported no bleeding.
- For children under 12 years of age treated prophylactically, the median annualized bleeding rate was 1.95 (Pathfinder™ 5). During the mean observation period of 182 days, 42% of the children reported no bleeding.

Safety

- The most frequently observed adverse events were skin problems (rash, erythema and pruritus) and local reactions at the injection site. The severity of all these reactions ranged from low to moderate.
- Severe adverse events associated with Esperoct™ administration (development of inhibitors, intervertebral disc infection, severe allergic reaction and increased symptoms of moderate bleeding) have been reported in four (4/270, or 1.5%) patients.
- Only one individual exposed to Esperoct™ for more than 50 days developed inhibitors out of a total of 235 (0.4%) patients previously treated prophylactically with at least one FVIII.
- One child (1/68, or 1.5%) developed antibodies to PEG following exposure to Esperoct™ in the Pathfinder™5 study with no clinical consequences.
- Nine individuals (9/270, or 3.3%) reported antibodies against a CHO cell antigen with no clinical consequences.

Efficiency

- Esperoct™, at the submitted price, is a least efficient treatment option compared to the other recombinant FVIIIs currently distributed in Quebec, namely Nuwiq™, Zonovate™ and Eloctate™.

Budget impact

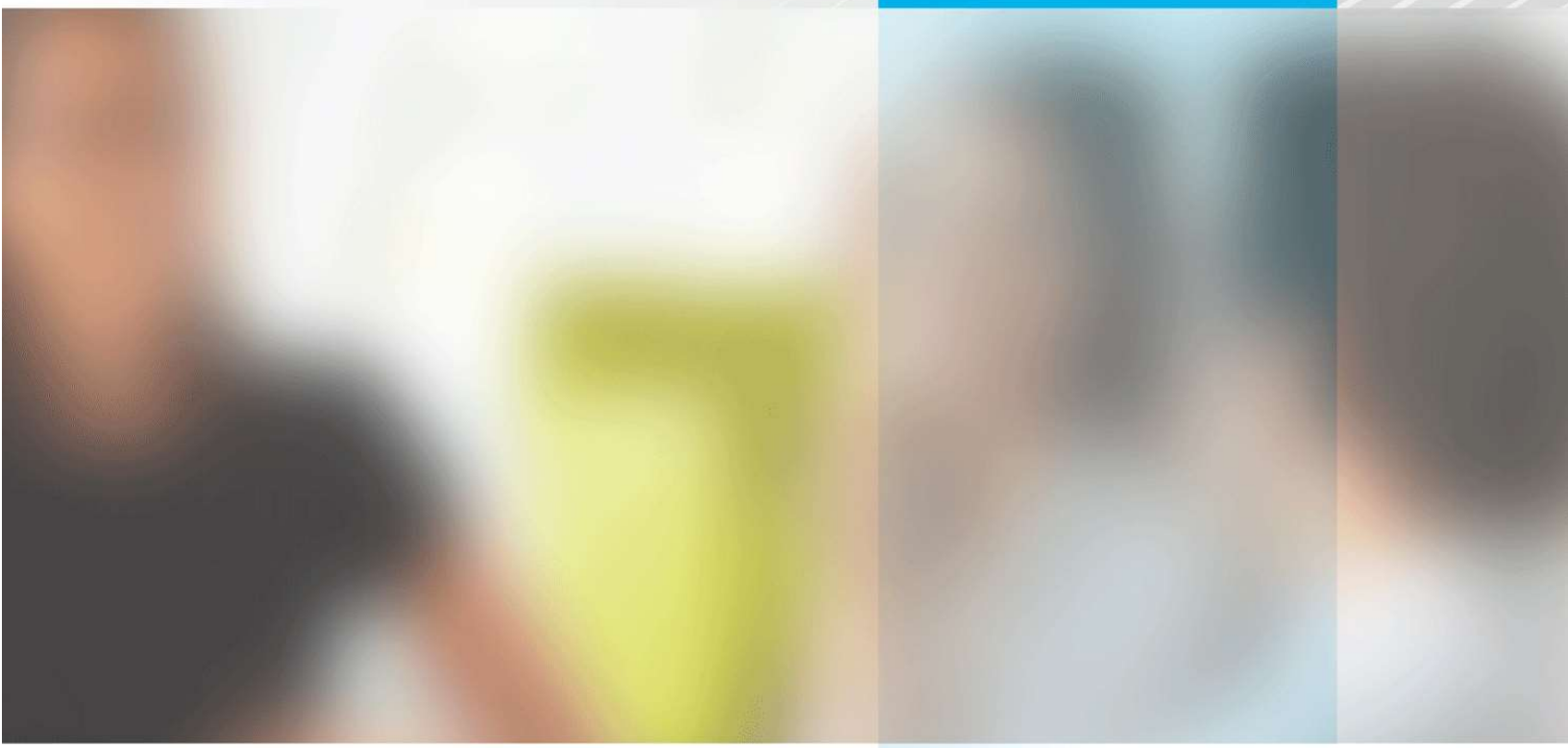
- Replacing Eloctate™, the only long-acting FVIII currently distributed in Quebec, with Esperoct™, at the submitted price, could lead to additional expenses estimated at $1.4 million over the next 3 years.

Deliberation concerning Esperoct™

The members of the Comité scientifique permanent de l'évaluation des médicaments aux fins d'inscription unanimously recognized the therapeutic value of turoctocog alfa pegol (Esperoct™) for routine prophylaxis, the on-demand treatment of bleeding episodes, and perioperative management in children and adults with hemophilia A. Consequently, the members unanimously share the opinion that turoctocog alfa pegol (Esperoct™) should be added to the *Liste des produits du système du sang du Québec*. However, they stress that, in the interest of equitable and reasonable access to treatments, this addition should be accompanied by measures aimed at reducing the economic burden so as not to create an incremental cost in relation to the currently distributed therapies.

Reasons for the unanimous position

- The annualized bleeding rate with prophylaxis and the hemostatic efficacy are comparable between Esperoct™ and the other recombinant FVIIIs.
- The product' safety is considered satisfactory, despite concerns regarding the immunogenicity of polyethylene glycol (PEG) and the accumulation of PEG in certain organs, especially in children.
- The costs of the prophylactic and on-demand treatments are significantly higher than those of the standard- and long-acting FVIII.
- Adding turoctocog alfa pegol (Esperoct™) to the *Liste des produits du système du sang du Québec* would increase treatment costs.



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