INESSS
LE SAVOIR PREND FORME

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Rebinyn™ (nonacog beta pegol) – Type B Hemophilia (re-evaluation)

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

Québec

SUMMARY

Rebinyn™ (nonacog beta pegol) – Type B Hemophilia (re-evaluation)

Mandate

At the request of the manufacturer Novo Nordisk Canada Inc., the *Institut national d'excellence en santé et en services sociaux* (INESSS) re-evaluated the blood system product Rebinyn™ (nonacog beta pegol), an intravenously injected recombinant factor IX (FIX) indicated in adults and children with hemophilia B (congenital factor IX deficiency or Christmas disease) for the control and prevention of bleeding episodes and in the perioperative setting as well as in patients 18 years and above with hemophilia B for routine prophylaxis to prevent or reduce the frequency of bleeding episodes.
The indications assessed for this re-evaluation are identical to those accorded by Health Canada.

INESSS previously evaluated nonacog beta pegol (evaluation of June 2020). During the first evaluation, INESSS issued an unfavourable recommendation for the addition of the product to the *Liste des produits du système du sang du Québec* because the therapeutic value had not been recognized by the Comité scientifique permanent de l'évaluation des médicaments aux fins d'inscriptions (CSEMI). This is the second evaluation of this product.

The following five FIX currently listed on the *Liste des produits du système du sang du Québec* were used as the comparators of nonacog beta pegol: BeneFIX™ (nonacog alfa; standard half-life recombinant FIX), Rixubis™ (nonacog gamma; standard half-life recombinant FIX), Alprolix™ (eftrénonacog alfa; extended half-life recombinant FIX), Idelvion™ (albutrepenonacog alfa; extended half-life recombinant FIX), Immunine™ (plasma-derived FIX).

Evaluation process

Published trials and manufacturer data were reviewed to document the efficacy, safety and efficiency of nonacog beta pegol. Experiential and contextual data from expert consultations and patients are presented as well.

Health need

Type B hemophilia is caused by a deficiency in FIX and is characterized by longer clotting times. In severe cases, FIX deficiency leads to frequent bleeding episodes in joints (hemarthrosis) and soft tissue in the absence of trauma. Prophylaxis with plasma or recombinant FIX is the preferred treatment. This consists of several weekly intravenous injections to replace the missing FIX.

Despite a good management of Quebecers living with type B hemophilia, the need for new treatment remains. In addition to permanent curative treatment, the following needs were identified by the experts consulted: better prevention of inhibitor development (neutralizing antibodies against FIX), prevention of hemophilic arthropathies and chronic pain, treatments that provide superior hemostatic protection that lasts longer and alleviates the stresses associated with repeated intravenous injections.

Results

Combined data from a real-world Canadian study, a post-market surveillance report on nonacog beta pegol, as well as previously evaluated clinical studies were considered for this evaluation.

Efficacy

- Nonacog beta pegol appears at least as effective as its comparators to prevent bleeding when used as a prophylactic.
- Nonacog beta pegol appears at least as effective as its comparators to treat breakthrough bleeds.
- In the studies listed, nonacog beta pegol demonstrates good or excellent hemostatic efficacy during surgery.

Safety

- The safety profile of nonacog beta pegol was considered acceptable.

Quality of life

- No new data regarding the impact of nonacog beta pegol on quality of life was presented.

Expert perspective

Considering the data presented as part of this reassessment, the expert consulted are of the opinion that the efficacy of nonacog beta pegol prophylaxis is comparable to the other FIX listed on the *Liste des produits du système du sang du Québec*. Experts also considered the safety profile of nonacog beta pegol to be similar to the other available therapeutic options for the targeted population. Furthermore, preoccupations regarding the potential accumulation of PEG in the choroid plexus remain theoretical in humans and would not prevent them from using nonacog beta pegol for the targeted population in Quebec.

Economic analysis

Efficiency analysis

- At the submitted price, nonacog beta pegol prophylaxis is the most efficient option of all extended half-life FIX but is less efficient than standard half-life FIX.

Budget impact analysis

- Replacing extended half-life FIX with nonacog beta pegol could lead to cost reductions for the next three years under current market conditions (same effective price of extended half-life FIX and access restriction).

Deliberation on the therapeutic value
A majority of members of the *Comité scientifique permanent de l'évaluation des médicaments aux fins d'inscription* (CSEMI) having exercised their right to vote are of the opinion that the therapeutic value of Rebinyn™ (nonacog beta pegol) is recognized for the treatment of hemophilia B (congenital factor IX deficiency or Christmas disease) in adults and children for the control and prevention of bleeding episodes and in the perioperative setting as well as in patients 18 years and above with hemophilia B for routine prophylaxis to prevent or reduce the frequency of bleeding episodes. **Reasons for the majority position** • Nonacog beta pegol meets albeit partially, the health need in the targeted population. • The supplementary data come from a Canadian study of low methodological quality but whose relevance to the Quebec context reassures committee members about the effectiveness of the product. • Nonacog beta pegol prophylaxis appears to be as effective as that FIX comparators, both standard half-life and extended half-life. • The safety profile is considered acceptable and comparable to other available options. • The new safety data together with the analyzes from the experts consulted reassured the members on the theoretical risk associated with the accumulation of PEG in the choroid plexus. • Nevertheless, the members deplore that the type of study and the methodologies used make it difficult to compare the different FIX with each other. **Reasons for the minority position** • Several standard half-life and extended half-life FIX are already listed on the *Liste des produits du système du sang du Québec*. • The lack of comparative data of good quality does not allow conclusions on the efficacy of nonacog beta pegol. • The uncertainty associated with the potential accumulation of PEG is specific to nonacog beta pegol and is therefore absent in the other FIX listed. • The magnitude of the health need addressed by nonacog beta pegol is considered low.

Deliberation on all the criteria

Members of the *Comité scientifique permanent de l'évaluation des médicaments aux fins d'inscription* (CSEMI) having exercised their right to vote are of the unanimous opinion that Rebinyn™ (nonagog beta pegol) should be added to the *Liste des produits du système du sang du Québec* for the treatment of hemophilia B (congenital factor IX deficiency or Christmas disease) in adults and children for the control and prevention of bleeding episodes and in the perioperative setting as well as in patients 18 years and above with hemophilia B for routine prophylaxis to prevent or reduce the frequency of bleeding episodes.

Reasons for the unanimous position

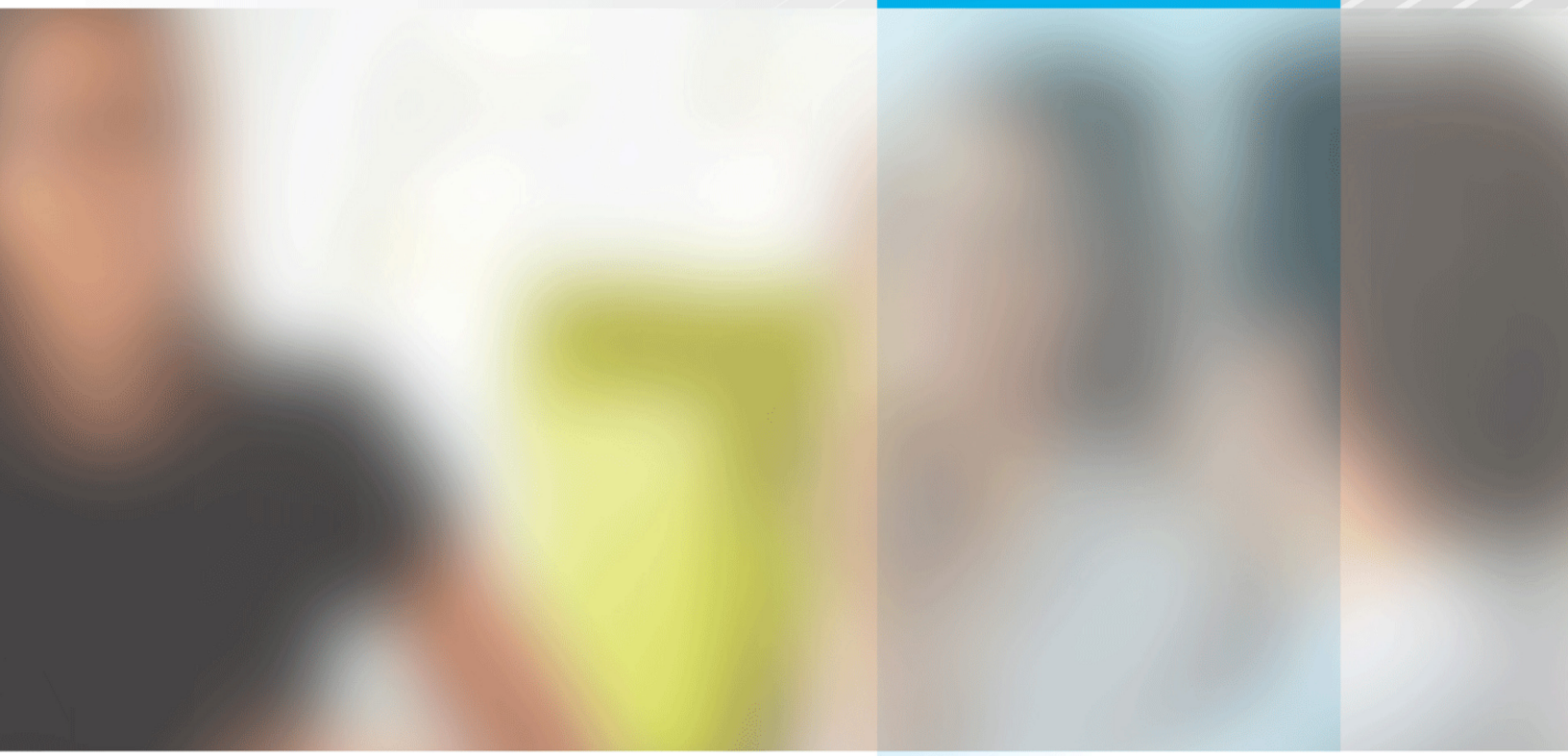
- Nonacog beta pegol prophylaxis appears to be as effective as that FIX comparators, both standard half-life and extended half-life.
- The use of nonacog beta pegol displays a low risk of adverse events for the target population.
- In a context of tender, the addition of nonacog beta pegol to the *Liste des produits du système du sang du Québec* represents a therapeutic alternative to other half-extended life products for the indicated population.
- Regarding the prophylactic use, the cost of nonacog beta pegol is [redacted] that standard half-life FIX and should be set at $ [redacted] per international unit. This corresponds to a reduction of at least [redacted]% to be considered equivalent to the cheapest standard half-life FIX.
- The cost of nonacog beta pegol is [redacted] of all extended half-life FIX.
- The addition of nonacog beta pegol to the *Liste des produits du système du sang du Québec* could reduce treatment costs by approximately $ 300,000 over three years.

Recommandations de l'INESSS sur le nonacog bêta pégol

In light of the available data, INESSS recommends that Rebinyn™ (nonacog beta pegol) be added to the *Liste des produits du système du sang du Québec* for the treatment of hemophilia B (congenital factor IX deficiency or Christmas disease) in adults and children for the control and prevention of bleeding episodes and in the perioperative setting as well as in patients 18 years and above with hemophilia B for routine prophylaxis to prevent or reduce the frequency of bleeding episodes.

Precision regarding the recommendation

From a distributive justice perspective, the reimbursement of nonacog beta pegol for the requested indication would constitute a responsible, fair and equitable decision if the cost of using nonacog beta pegol does not exceed that of extended half-life FIX during the next call for tenders.



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