INESSS
LE SAVOIR PREND FORME

JUNE 2020

Rebinyn™ (nonacog beta pegol) – coagulation factor IX (recombinant)

English summary

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

Direction de l'évaluation des médicaments et des technologies à des fins de remboursement

Québec

SUMMARY

Rebinyn™ (nonacog beta pegol) – coagulation factor IX (recombinant)

Mandate

The Institut national d'excellence en santé et en services sociaux (INESSS) 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 following four recombinant FIX, currently indicated for the treatment of hemophilia B and listed in the *Liste des produits du système du sang du Québec,* served as comparators: BeneFIX™ (nonacog alfa), Rixubis™ (nonacog gamma), Alprolix™ (eftrenonacog alfa) et Idelvion™ (albutrepenonacog alfa).

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

Hemophilia B is an X chromosome-linked recessive genetic disease characterized by coagulation factor IX (FIX) deficiency. This deficiency prolongs coagulation times, which can lead to frequent bleeding episodes in the joints (hemarthrosis), muscles and mucus membranes. Some bleeding events can also lead to severe motor handicaps or even be life-threatening.

The current FIX replacement therapies enable Quebecers who are type B hemophiliacs to prevent or stop their bleeding episodes. Experts and patients were queried about health needs in the hemophilia B community. Treatments that better prevent the development of inhibitors, hemophiliac arthropathies and chronic pain, and therapies that provide superior, longer-lasting hemostatic protection with fewer intravenous injections were among the needs mentioned most frequently.

Results

Efficacy

The efficacy evaluation for nonacog beta pegol was based on four phase III, open-label and non-controlled trials. As a result of the restriction of the indication, efficacy results for the prophylactic use of nonacog beta pegol in children and adolescents under 18 years f age were not considered. The overall efficacy evidence was considered very low.

- The prophylactic dose of 40 IU/kg every seven days showed lower median and mean annual bleeding rates compared to the 10 IU/kg dose.
- The majority of bleeding events satisfied the hemostatic efficacy criteria and most of them required a single injection of nonacog beta pegol.
- Only one severe bleeding event was treated with nonacog beta pegol.
- The hemostatic efficacy of the 34 surgeries for which efficacy results were available was considered good or excellent.

Safety

The safety of nonacog beta pegol was evaluated across six clinical studies. A total of 115 unique patients received at least one injection of nonacog beta pegol. The evidence level for the safety results was considered very low.

- PEG accumulation in the choroid plexus and vacuolation of epithelial cells of the choroid plexus were observed in animals during preclinical trials.
- The most frequent adverse events observed during the clinical trials were injection site reaction (observed in 3.5 % of subjects) and pruritus (2.6 %).
- A single case of hypersensitivity reaction was reported and led to the subject's withdrawal.
- No subject developed anti-FIX antibodies.

Impact of the drug on patients' quality of life

- Quality of life improvement was found by the HAEMO-QOL-III and HAEM-A-QOL surveys for individuals treated weekly with the 40 IU/kg dose ("feeling" and "sport" domains) and people treated on-demand ("view" domain).

Expert perspective

- The experts consulted consider that the hemostatic efficacy of nonacog beta pegol, for the requested indications, is considered similar to its recombinant FIX comparators.
- While some experts mentioned the impossibility of evaluating the efficacy of nonacog beta pegol to treat severe bleedings, others indicated that the overall efficacy evidence is enough to conclude that the product is similar to its comparators.
- According to the experts consulted, the safety profile of nonacog beta pegol during the clinical trials is considered comparable to its recombinant FIX comparators.

- Nonetheless, PEG accumulation in the brain of animals during the preclinical trials was considered a considerable risk and some experts mentioned they would not recommend nonacog beta pegol for children.

Deliberation on nonacog beta pegol

Deliberation on Rebinyn™

Members of the *Comité scientifique permanent de l'évaluation des médicaments aux fins d'inscription* (CSEMI) unanimously share the opinion that the therapeutic value of Rebinyn™ (nonacog beta pegol) has not been demonstrated 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.

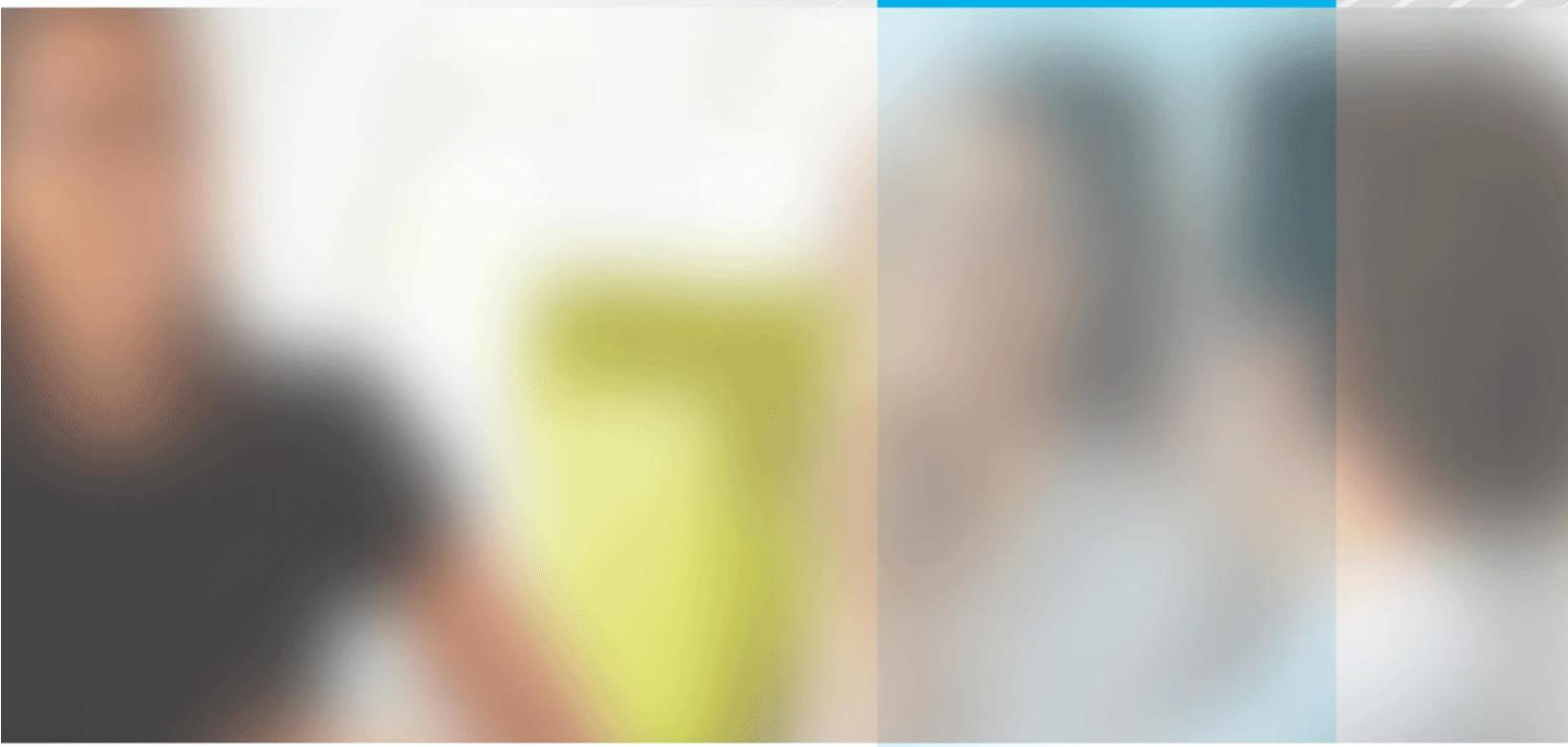
Reasons for the unanimous position

Members of the Committee recognized the considerable burden associated with the disease. They also recognized that the reduced injection frequency is considered an advantage for patients. Nevertheless, after careful examination of all the evidence, the following observations were made:

- Given the weakness of the evidence, the available studies do not permit us to conclude that the therapeutic value of nonacog beta pegol is noninferior to that of the other recombinant FIXs currently available;
- Concerns were raised by the members of the CSEMI regarding the accumulation of PEG in the brain of animals during preclinical studies as well as the potential risks associated with long term deposits of PEG;
- Considering the availability of safer therapeutic options, the members advise caution.

INESSS' recommendation regarding Rebinyn™

In light of the available data, INESSS recommends that Rebinyn™ (nonacog beta pegol) not be added to the *Liste des produits du système du sang du Québec* since the product's therapeutic value has not demonstrated. Additional efficacy and safety data with a higher level of evidence are required to support the therapeutic value for the proposed indications.



Siège social

2535, boulevard Laurier, 5e étage
Québec (Québec) G1V 4M3
418 643-1339

Bureau de Montréal

2021, avenue Union, 12e étage, bureau 1200
Montréal (Québec) H3A 2S9
514 873-2563
inesss.qc.ca

Institut national d'excellence en santé et en services sociaux
Québec