INESSS
LE SAVOIR PREND FORME

FEBRUARY 2023

Rebinyn™ – Prophylaxis in children and adolescents with hemophilia B

English summary

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

Québec

SUMMARY

Rebinyn™ – Prophylaxis in children and adolescents with hemophilia B

Mandate

At the request of the manufacturer, Novo Nordisk Canada Inc., the Institut national d'excellence en santé et en services sociaux (INESSS) evaluated Rebinyn™ (nonacog beta pegol), a pegylated recombinant human factor IX (FIX). In Canada, nonacog beta pegol is indicated for the control and prevention of bleeding episodes, the control and prevention of bleeding in the perioperative setting, and routine prophylaxis in adults and children with hemophilia B (congenital FIX deficiency, otherwise known as Christmas disease). This evaluation concerns the use of nonacog beta pegol "*as routine prophylaxis in children and adolescents under 18 years of age with hemophilia B to prevent or reduce the frequency of bleeding episodes*."

Nonacog beta pegol was previously evaluated twice by INESSS for occasional use in adults and children for bleeding and as routine prophylaxis in adults. This is the third evaluation of this product and is focused on the use of nonacog beta pegol for the indication of long-term prophylaxis in children and adolescents.

Evaluation process

Literature data and the data provided by the manufacturer were reviewed to evaluate the efficacy, safety and cost-effectiveness of nonacog beta pegol. In addition, contextual and experiential data from expert consultations were mobilized and integrated.

Populational dimension

Hemophilia B is a rare and serious genetic disorder caused by coagulation FIX deficiency. The severe forms of the disorder manifest as spontaneous and recurrent bleeding that can lead to significant joint damage (hemarthrosis) and disability. In Québec, there are 83 patients being treated for a moderate or severe hemophilia B phenotype, approximately 19 of whom are children or adolescents under 18 years of age.

FIX replacement prophylaxis is the standard of care for type B hemophiliacs with a severe phenotype and is started around the age of 1 year. It consists of several weekly intravenous injections of FIX to prevent hemarthrosis and other spontaneous bleeding. Five replacement FIXs, including two long-acting products (Alprolix™ and Idelvion™), are currently listed on the *Liste des produits du système du sang du Québec* and indicated as routine prophylaxis in children. For about the past year, the lifting of restrictions on access to extended half-life FIXs has enabled type B hemophiliacs aged 12 years and under on long-term prophylaxis to have unrestricted access to FIX prophylaxis with Alprolix™.

Despite the fact that hemophilia B is well managed in Québec, the health need is only partially met by the current treatments. In addition to the desire for a permanent curative treatment, there is a need for a treatment that would be less burdensome to administer. Treatments that offer better prevention of hemophilic arthropathies, chronic pain and the development of inhibitors are also desirable.

Clinical dimension

The main efficacy and safety data for nonacog beta pegol for use as routine prophylaxis in children with hemophilia B are based on two open-label, uncontrolled phase III pivotal studies. Although these studies were considered to be of moderate methodological quality, the risk of design bias is significant. Overall, the quality of the efficacy and safety evidence for nonacog beta pegol for use as routine prophylaxis in children and adolescents with hemophilia B was considered very low. A Canadian study in a real-life care setting that included some pediatric patients were also considered.

Efficacy

- The results of the two pivotal studies indicate that the use of nonacog beta pegol as routine prophylaxis is effective in maintaining a low annualized bleeding rate (ABR) in children.
- Based on the Canadian real-world retrospective study and the expert perspective, nonacog beta pegol appears to be at least as effective as its comparators.

Safety

- Based on the results of the pediatric clinical studies, the safety profile of nonacog beta pegol is considered acceptable and appears to be comparable to that of other options on the *Liste*.
- In animal toxicology studies, the administration of high doses of nonacog beta pegol was associated with polyethylene glycol (PEG) deposition in certain organs surrounding the central nervous system, with no observable short-term clinical consequences.

Expert perspective

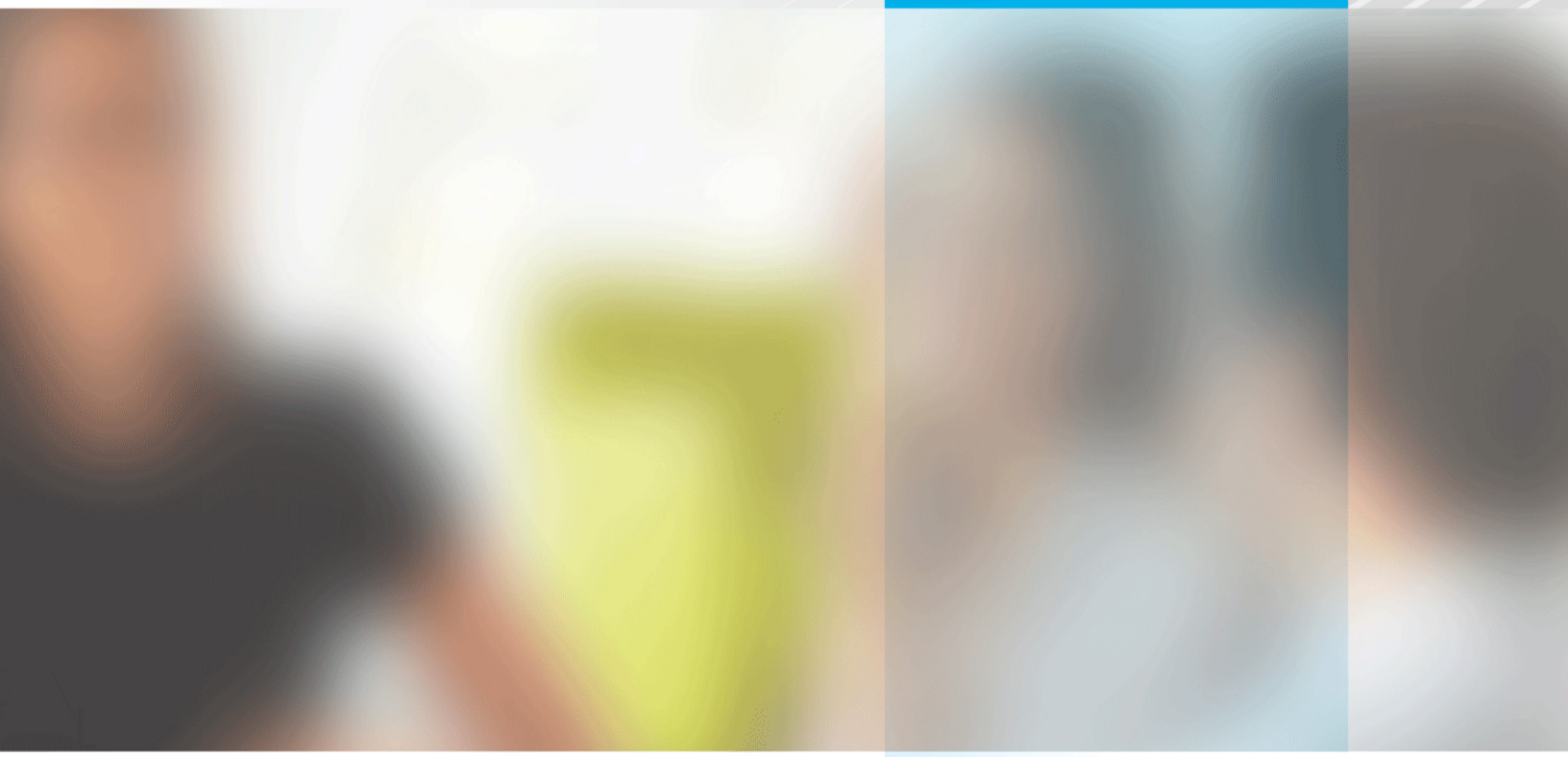
- Based on the results of the pivotal studies, the experts feel that the efficacy and safety profiles of nonacog beta pegol in children are satisfactory and similar to those of the other available treatments.
- However, the experts consider that the theoretical risks associated with the possible accumulation of PEG in different developing structures and organs in children raise a significant uncertainty regarding the drug's long-term safety.
- As for its use in children, the experts indicate a preference for the other FIXs on the *Liste*, given that they are effective, safe and theoretically risk-free treatment options.

Sociocultural dimension

Expert perspective

- In Québec, children with hemophilia B and their families are involved in choice-of-treatment decisions and receive from health professionals all the information they need to make free and informed decisions.
- In this context, being aware of the potential risks associated with PEG and of the other available treatment options, the experts anticipate a low propensity among parents to choose Rebinyn™ as treatment for their hemophilic children.

Deliberation regarding therapeutic value
A majority of the members of the *Comité scientifique permanent de l'évaluation des médicaments aux fins d'inscription* having exercised their right to vote are of the opinion that the therapeutic value of Rebinyn™ has not been demonstrated for its use as routine prophylaxis in children and adolescents under 18 years of age with hemophilia B to prevent or reduce the frequency of bleeding episodes. **Reasons for the majority opinion** ▪ The members are sensitive to the needs of young type B hemophiliacs. However, they feel that nonacog beta pegol only partially meets their health needs. ▪ Based on the study results and the perspective of the experts consulted, the members recognize the efficacy of long-term prophylaxis with nonacog beta pegol as being similar to that of the other recombinant FIXs. ▪ However, several members called attention to the pivotal studies' methodological weakness. In their opinion, the current data do not support considering nonacog beta pegol's therapeutic value to be comparable to that of the other products on the *Liste*. ▪ Although the clinical study data show an acceptable short-term safety profile, the members are concerned about the risks associated with PEG deposition in different developing organs and structures in children who would use nonacog beta pegol as lifelong routine prophylaxis. ▪ Given that there are other therapeutic options that are considered effective and safe, the members urge caution. **Reasons for the minority position** ▪ According to some of the members, the risks associated with PEG depositions are theoretical. In this regard, they indicated that there is no empirical evidence to suggest that nonacog beta pegol is less well tolerated or more toxic than the other recombinant FIXs.
INESSS's recommendation regarding Rebinyn™
In light of the available data, INESSS does not recommend including Rebinyn™ on the *Liste des produits du système du sang du Québec* for routine prophylaxis in children and adolescents under 18 years of age with hemophilia B.



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