INESSS
LE SAVOIR PREND FORME

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Vonvendi[MC] (vonicog alfa) Recombinant von Willebrand factor – von Willebrand disease

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

SUMMARY

Vonvendi™ (vonicog alfa) Recombinant von Willebrand factor – von Willebrand disease

Mandate

The Institut national d'excellence en santé et en services sociaux (INESSS) evaluated the blood system product Vonvendi™ (vonicog alfa, BAX 111), an intravenously injected recombinant von Willebrand factor (rVWF) for the treatment and control of bleeding episodes and the perioperative management of bleeding in adults (age ≥ 18) diagnosed with von Willebrand disease.

The products Humate-P™ and Wilate™, currently indicated as VWF/factor VIII (FVIII) replacement therapies and listed in the *Liste des produits du système du sang du Québec*, served as comparators.

Evaluation process

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

Health need

Von Willebrand disease is caused by a quantitative or qualitative VWF defect with or without a secondary FVIII deficiency. These deficiencies result in prolonged spontaneous or traumatic bleeding, usually mucocutaneous, which can sometimes be life-threatening.

In Québec, von Willebrand disease treatment needs are, in general, adequately addressed with the current therapeutic strategies. Most patients respond well to first-line treatment, desmopressin (DDAVP™), but not all to the same extent. In cases of an ineffective response or a contraindication to DDAVP™, patients have access to a plasma-derived VWF/FVIII concentrate, Humate-P™.

Results

Efficacy

The results are based on two Phase III studies (one per indication) with few patients and no direct comparison between vonicog alfa and its comparators. The level of evidence was considered very low.

<u>On-demand treatment (22 patients; maximum follow-up of 12 months)</u>

- Although hemostatic efficacy was rated 'excellent' or 'good' for 100% of the bleeding episodes, most were minor, and only seven major bleeds were assessed.
- 81.8% (157/192) of the bleeding episodes (mostly minor, 113/157) were resolved with a single infusion of vonicog alfa combined with recombinant FVIII.

Perioperative prophylaxis (15 surgeries in 15 patients)

- Hemostatic efficacy was rated ‘excellent’ or ‘good’ for 100% of the surgeries.
- 67% (10/15) of patients did not require FVIII before, during or after their surgery. This result can be explained in large part by the fact that patients were managed earlier by receiving two preoperative doses of vonicog alfa (12-24 hrs and 3 hrs before the procedure), which enabled them to produce sufficient levels of endogenous FVIII.
- 60% (3/5) of patients with type 3 who underwent major surgery received FVIII before their operation.
- The mean actual intraoperative blood loss was 30% lower than predicted, [redacted].

Safety

- The most frequently reported adverse events were nausea, vomiting, dizziness, vertigo and generalized pruritus.
- Three serious adverse events related to vonicog alfa were observed in two patients (chest discomfort, increased heart rate and deep-vein thrombosis).
- A second case of deep-vein thrombosis was reported after the product was introduced on the market.
- The development of neutralizing antibodies to the drug or its components was not reported in any of the 80 participants in the clinical studies.

Impact of the drug on the patients’ quality of life

- The patients surveyed who had been exposed to vonicog alfa in the context of on-demand treatment or perioperative prophylaxis reported that the drug had [redacted] impact on their quality of life.

Experts’ perspective

- The experts consulted deplored the level of evidence and the quality of the studies used to demonstrate the efficacy and safety of vonicog alfa (number of Phase III studies, very small number of patients, short patient follow-up and open-label and non-randomized controlled clinical trials).
- Despite the small number of patients and the short follow-up, the efficacy and safety of vonicog alfa appear, based on the available data, to be similar to what is expected for plasma-derived VWF.
- The experts consulted expressed concern about the high concentration of high-molecular-weight VWF multimers, which could increase the risk of thrombosis, particularly in individuals with low levels of the enzyme ADAMTS13.
- They indicated that von Willebrand disease patients in Québec are very well-managed with the current treatments, whose safety is supported by many years of use. According to these experts, vonicog alfa does not fulfill a therapeutic need for a specific von Willebrand disease population.

- However, the experts consulted acknowledged that, in theory, vonicog alfa would be useful in individualizing treatment in cases of elective surgery. However, they expressed concern about the considerable increase in complexity that two separate products (vonicog alfa and rFVIII), as opposed to one (Humate-P™ or Wilate™), could cause when managing products or self-medication at home, in hospitals or at distribution centres.
- Considering the current management, the very low level of the evidence presented and the degree of uncertainty surrounding the use of the product in real-world care settings, the experts consulted do not see vonicog alfa offering any benefit to the healthcare system.

Deliberation regarding vonicog alfa

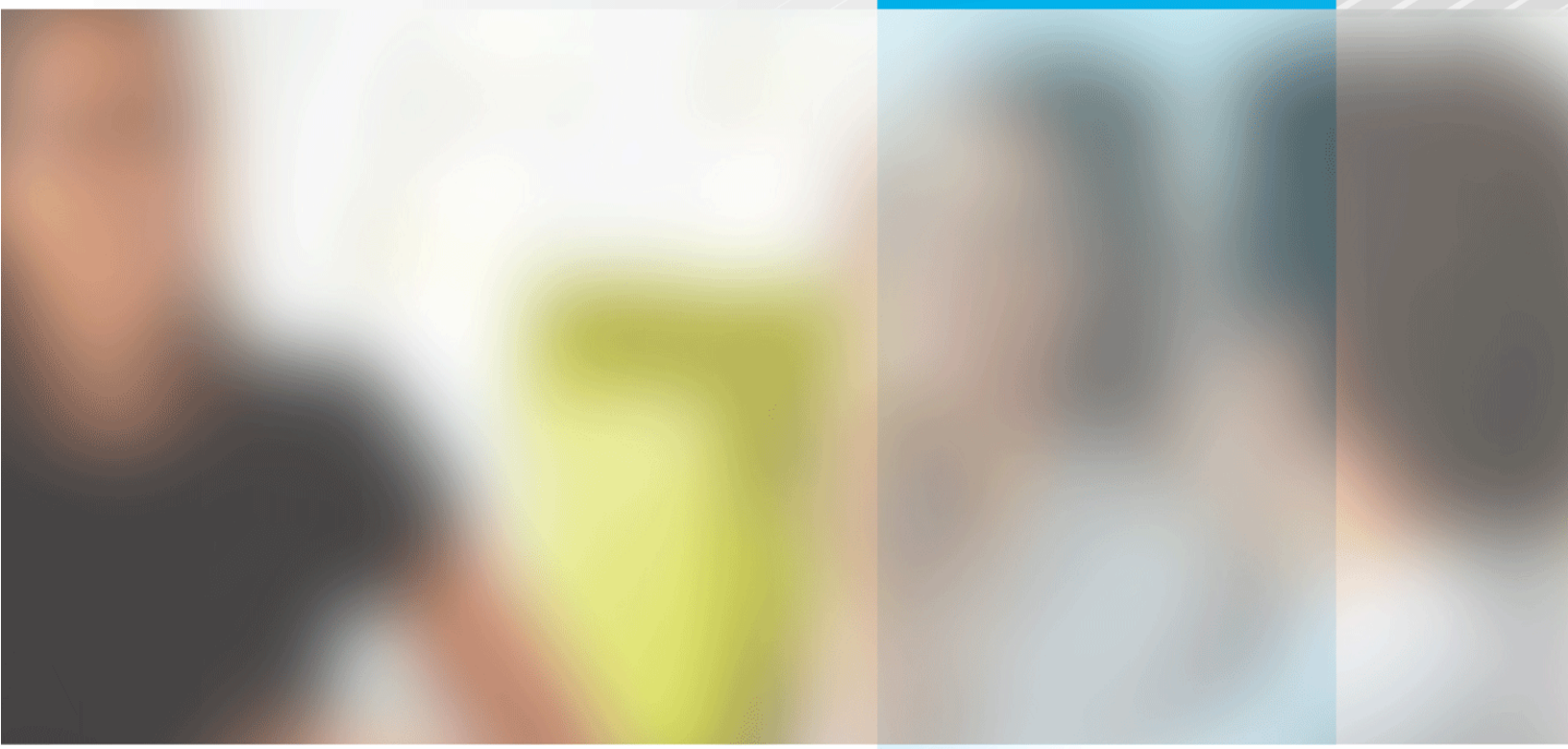
The members of the Comité scientifique permanent de l'évaluation des médicaments aux fins d'inscription (CSÉMI) unanimously shared the opinion that the therapeutic value of Vonvendi™ (vonicog alfa) has not been demonstrated for the treatment and control of bleeding episodes or the management of perioperative bleeding in adults (age ≥ 18) diagnosed with von Willebrand disease.

Reasons for the unanimous position

- The level of evidence for vonicog alfa is very low and is based on limited clinical data. In the absence of a comparative study with VWF/FVIII concentrates actively used in current practice, the Committee's members found it difficult to recognize vonicog alfa as being noninferior in terms of therapeutic value.
- The degree of uncertainty regarding vonicog alfa's safety.
- Concerns were raised about the management and the use of vonicog alfa in real-world care settings. Individualizing treatment involving vonicog alfa would render patient management and perioperative management significantly more complex.
- Vonicog alfa has emerged in Québec at a time when therapeutic management is already largely accomplished with desmopressin (DDAVP™) and VWF/FVIII concentrates, which cover a wide range of clinical scenarios.

INESSS's recommendation regarding vonicog alfa

In light of the available data, INESSS recommends that Vonvendi™ (vonicog alfa) not be added to the *Liste des produits du système du sang du Québec*. More data are needed to support the recognition of its therapeutic value.



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