INESSS
LE SAVOIR PREND FORME

OCTOBER 2019

Alphanate[MC] - von Willebrand disease
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 Comité scientifique permanent d'évaluation des médicaments aux fins d'inscription de l'Institut national d'excellence en santé et en services sociaux (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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Dépôt légal

Bibliothèque et Archives nationales du Québec, 2019
Bibliothèque et Archives Canada, 2019
ISSN 1915-3104 INESSS (PDF) ISBN 978-2-550-85077-9 (PDF)

Pour citer ce document : Institut national d'excellence en santé et en services sociaux (INESSS). Alphanate[MC] – Maladie de von Willebrand. Rapport rédigé par Carole Campion, Richard Bisaillon et Léon Nshimyumukiza. Québec, Qc : INESSS; 2019. 31 p.

L'Institut remercie les membres de son personnel qui ont contribué à l'élaboration du présent document.

SUMMARY

Alphanate™ - von Willebrand disease

Mandate

The Institut national d'excellence en santé et en service sociaux (INESSS) carried out an evaluation of Alphanate™, an intravenously injected vWF/FVIII concentrate for the prevention and treatment of mild and/or non-life-threatening bleeding episodes or surgical bleeding in adults and pediatric patients with von Willebrand disease (vWD), when desmopressin (DDAVP™) is known or suspected to be either ineffective or contraindicated. Alphanate™ is not indicated for patients with severe vWD (type 3) undergoing major surgery.

Evaluation process

Literature data and data provided by the manufacturer were reviewed to document the efficacy, safety and efficiency of Alphanate™. Experiential and contextual data from expert consultations are presented as well.

Health need

vWD is the most common hereditary bleeding disorder. It is characterized by a primary deficiency of vW factor (vWF) with or without a secondary deficiency of FVIII. The disease is classified into types 1, 2 and 3, based on the reduced levels and functional activity of vWF. The location and severity of the bleeding varies considerably according to the type of vWD. The bleeding can be mucocutaneous or affect deep tissues, such as joints and muscles, and can lead to tissue destruction or permanent sequelae.

Management is based on the normalization of vWF and FVIII during bleeding episodes, perioperative prophylaxis and long-term prophylaxis. In Québec, first-line treatment consists of the intravenous administration of an analogue of the antidiuretic hormone vasopressin, DDAVP™, which is generally used to prevent or treat mild to moderate bleeding. In cases of more severe vWD, or when DDAVP™ is ineffective or contraindicated, replacement therapy with a vWF/FVIII plasma concentrate is administered intravenously.

In Québec, it is estimated that approximately 600 patients have vWD, with the following breakdown: 540 type 1, 40 type 2 and 20 type 3. Most patients respond to DDAVP™. Otherwise, the plasma-derived vWF/FVIII concentrate Humate-P™, which is on the *Liste des produits du système du sang du Québec*, effectively treats all types of bleeding. Wilate™ is another vWF/FVIII concentrate figuring on this list, but it is not currently distributed.

Results

Efficacy

Two clinical studies were selected: a prospective pivotal study and a retrospective study. [redacted] of the bleeding episodes ([redacted]%) in the pivotal study were completely controlled with one or two injections of Alphanate™, in the absence of use of cryoprecipitates, alternate vWF/FVIII concentrate, or platelet infusion. In the prevention of bleeding in a surgical or invasive procedure context, [redacted] of surgical procedures ([redacted]%) in the pivotal study did not generate intraoperative blood loss greater than 1.5 times the predicted value, and 93.5% of surgeries in the retrospective study had a hemostatic response rated as "excellent/good". Out of 132 evaluated procedures (combined results of the pivotal and the retrospective study), [redacted] surgeries/invasive procedures had a clinical response below expectations and required blood transfusions in some cases to achieve hemostasis. A total of 18 pediatric patients were evaluated in the pivotal study. According to Health Canada, the observed results were comparable to those for adult patients.

Quality of evidence: very low

Safety

No serious treatment-related adverse events, deaths or study discontinuations were observed in the two studies evaluated. The pediatric population evaluated is considered small. A larger pediatric population should be studied.

Quality of evidence: very low

Quality of life

No study evaluating the impact of Alphanate™ on quality of life was identified.

Therapeutic value

Given the available clinical results, and in the absence of comparative studies, the experts consulted believe that Alphanate™ has a clinical efficacy equivalent to that of the other plasma-derived products Humate-P™ and Wilate™. However, most of these experts maintain that the restriction of Alphanate™ to cases of minor or non-life-threatening bleeding imposed by Health Canada, is a major handicap, as these needs are already being met with DDAVP™. Alphanate™ is therefore being marketed in a context where Humate-P™ is already meeting all the needs in the management of vWD when DDAVP™ is ineffective or contraindicated, and this, in a wide range of clinical scenarios. The Groupe d’experts sur les produits du système du sang concluded that, although Alphanate™ has a potentially similar clinical profile to Humate-P™ and Wilate™, there is no role for it in the current therapeutic strategy in Québec.

Deliberation concerning Alphanate™

The members of the Comité scientifique permanent de l'évaluation des médicaments aux fins d'inscription (CSEMI) did not, unanimously, recognize the therapeutic value of Alphanate™ for the indication issued by Health Canada:

Prevention and treatment of mild and/or non-life-threatening bleeding episodes or surgical bleeding in adult and pediatric patients with von Willebrand disease, when desmopressin (DDAVP ™) is known or suspected to be either ineffective or contraindicated.

Consequently, the committee's members were unanimously of the opinion that Alphanate™ should not be added to the *Liste des produits du système du sang du Québec*.

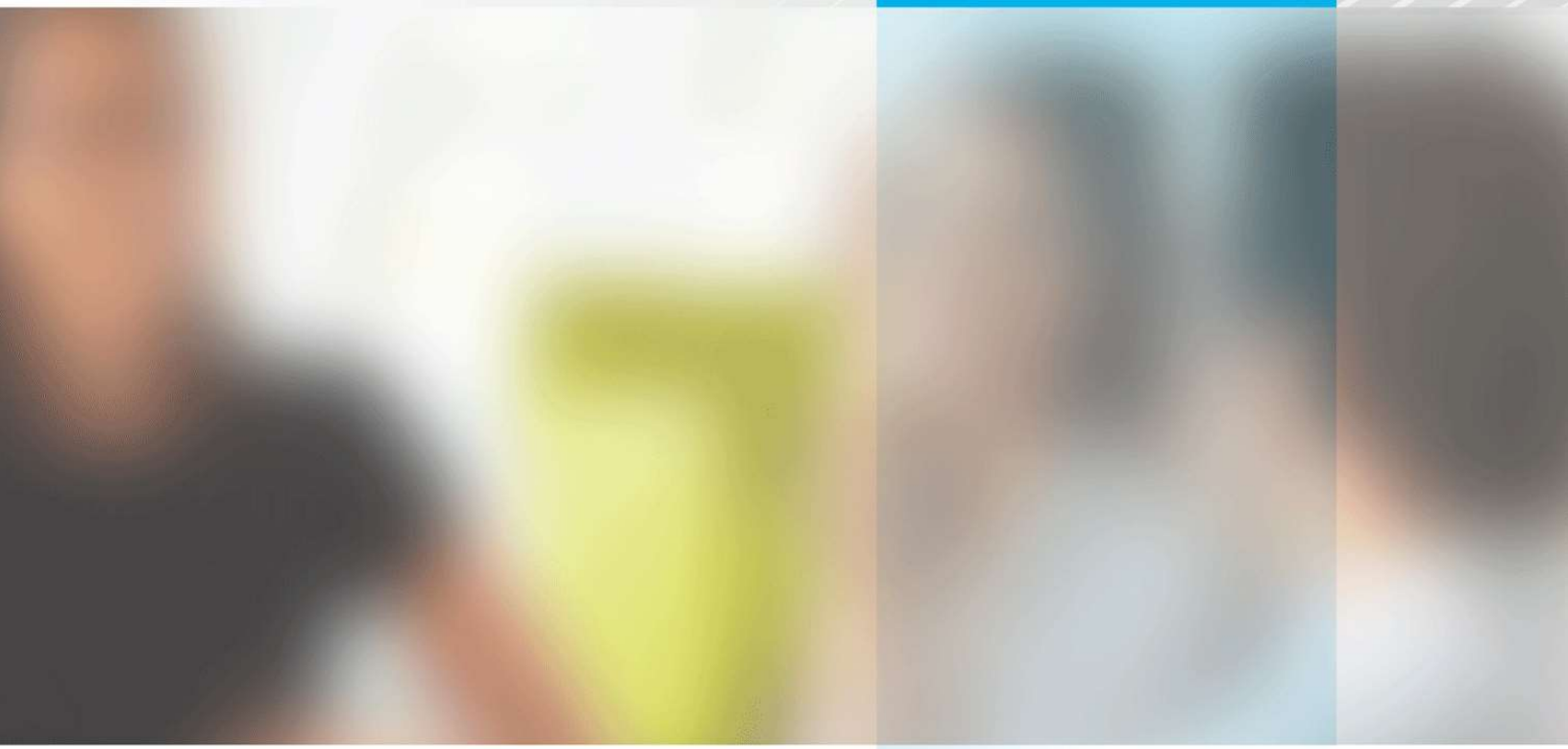
Reason for the unanimous position

- Despite the fact that this product has been on the market for several years, the clinical data are limited and of poor quality.
- There are no comparative studies comparing Alphanate™ with the other vWF/FVIII concentrates, Humate-P™ and Wilate™. Based on the available studies, the comparators have [redacted] hemostatic efficacy [redacted] Alphanate™ for on-demand treatment and comparable hemostatic efficacy for perioperative prophylaxis.
- Given Health Canada's restriction on the indication, Alphanate™ is intended for a very limited population at a time when, in Québec, therapeutic management is already being done mostly with desmopressin (DDAVP™) or Humate-P™, which covers a wide range of clinical scenarios.
- It is difficult to justify a role for this product in the therapeutic arsenal currently available for patients with von Willebrand disease.

INESSS's recommendation

In the light of the available data, INESSS does not consider it relevant to add Alphanate™ to the *Liste des produits du système du sang du Québec* for the prevention and treatment of mild and/or non-life-threatening bleeding episodes or surgical bleeding in adults and pediatric patients with von Willebrand disease, when desmopressin (DDAVP™) is known or suspected to be either ineffective or contraindicated.
The indication for Alphanate™ is too limited to grant it a role in the current therapeutic strategy in Québec.

ménorragies, des hémorragies et des douleurs abdominales ont été observées. Un cas de décès jugé non lié au traitement par Humate-P^{MC} est survenu dans l'une des études [Lillicrap *et al.*, 2002; Dobrkovska *et al.*, 1998]. Le suivi d'un traitement a dû être arrêté



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