HAUTE AUTORITÉ DE SANTÉ

HAEMATOLOGY
New indication
June 2016

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

VONCENTO (human coagulation factor VIII + von Willebrand factor)

No clinical benefit demonstrated in prophylaxis of bleeding episodes of von Willebrand disease.

Main points

- VONCENTO has Marketing Authorisation in prophylaxis of bleeding episodes regardless of the patient's age, in the treatment of bleeding episodes or in prophylaxis and treatment of surgical bleeding in patients aged < 12 years with von Willebrand disease.
- Clinical data on its efficacy and safety represent a low level of evidence.

Pre-existing indications*

- VONCENTO already has Marketing Authorisation in prophylaxis and in treatment of haemophilia A (congenital factor VIII deficiency), surgical bleeding and treatment of bleeding episodes in patients over 12 years of age with von Willebrand disease, when desmopressin treatment alone is ineffective or contraindicated.

Therapeutic use

- Treatment of bleeding episodes, prophylaxis and treatment of surgical bleeding in patients under 12 years of age: administration of von Willebrand factor (VWF) concentrate is recommended when desmopressin cannot be used. The choice between administration of a VWF concentrate and a concentrate combining VWF and factor VIII depends on the clinical context and on the urgency of the need to normalise haemostasis.
- Prophylaxis of bleeding episodes in von Willebrand disease: a prophylactic treatment with concentrates combining VWF and FVIII or a von Willebrand concentrate without FVIII can be considered in patients with a severe form of von Willebrand disease and recurrent bleeding localized at critical sites (gastrointestinal bleeding, haemarthrosis, recurrent epistaxis in children).
- **Role of the medicinal product in the therapeutic strategy**
  VONCENTO has a role in second-line therapy in the treatment of bleeding episodes, prophylaxis and treatment of surgical bleeding in patients with von Willebrand disease under 12 years of age, when desmopressin is contraindicated or ineffective. In long-term prophylaxis, VONCENTO is an alternative to WILFACTIN in patients aged ≥ 6 years. There is no alternative to VONCENTO in the long-term prophylactic treatment of children below the age of 6 years.

Clinical data

- An open-label phase III study sought to evaluate the haemostatic efficacy and the safety of VONCENTO in prophylaxis and in treatment of patients under 12 years of age. It included 17 children under 12 years of age treated in prophylaxis (n=4) or in on-demand treatment (n=13). In the 12 months prior to enrolment, the 4 patients had an average of 14.3 bleeding events, including 9.3% being severe events. During the year of prophylaxis with VONCENTO, the mean number of bleeding episodes of a non-surgical origin was 22.8 (± 13.2) events per patient on average, of which 0.8% were severe on average, while having received 111 infusions. The haemostatic efficacy was rated excellent (80.8%) or good (19.2%) for the 73 bleeding episodes treated. No patient treated in

* This summary does not cover these indications.

prophylaxis underwent surgery. The results of this sub-group of children treated in prophylaxis did not demonstrate the efficacy of the prevention of bleeding by VONCENTO.

- A follow-up study included 17 patients from a study in adults and adolescents over 12 years of age and 3 children under 12 years, with a follow-up of about 2 years. Ten patients were treated in prophylaxis, with a mean follow-up of about 22 months. The 10 patients included in the prophylaxis group presented with a total of 118 bleeding episodes, of which 96 (81.4%) were treated with VONCENTO. For one patient treated in prophylaxis, no bleeding was observed. The bleeding was mostly mucosal bleeding (88.1%). Twelve (10.2%) severe bleeding episodes occurred in 7 patients, including 5 episodes of severe mucosal bleeding in 4 patients. No bleeding required the patient to be hospitalised. Four patients treated in prophylaxis underwent a minor surgical procedure.
- The studies do not provide any information about the course of administration of factor VIII during long-term prophylaxis, while the Marketing Authorisation contains a warning about the risk of an excessive increase in factor VIII level that may increase the risk of thrombotic events. Regarding the low number of patients treated in prophylaxis for at least a year, no thrombotic episode has been reported.
- Although available clinical data do not demonstrate the effectiveness of prophylaxis, clinical practice in some patients justifies the use of this therapeutic modality (often ineffective in repeated gastrointestinal bleeding).

Special prescribing conditions

- Medicinal product derived from human blood.
- Medicine for hospital prescription

Benefit of the medicinal product

- The actual clinical benefit* of VONCENTO is substantial.
- VONCENTO does not provide any improvement in actual clinical benefit** (IACB V) compared to its clinically relevant comparator in prophylaxis of bleeding episodes in von Willebrand disease. In the extension of the indication to the treatment of bleeding episodes or to prophylaxis and treatment of surgical bleeding in children < 12 years of age with von Willebrand disease, the improvement in actual clinical benefit initially granted in patients aged ≥ 12 years (IACB V) has not changed.
- Recommends inclusion on the list of reimbursable products for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 08 June 2016 (CT-15030) and is available at **www.has-sante.fr**

* The actual clinical benefit (ACB) of a medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the ACB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

** The improvement of actual clinical benefit (IACB) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of IACB on a scale from I (major) to IV (minor). A level V IACB (equivalent of “no IACB”) means "no clinical added value".