AWTTC
All Wales Therapeutics & Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

Vonicog alfa (Veyvondi®▼) for on-demand treatment of non-surgical and surgical (elective and emergency) bleeding episodes in children aged up to 17 years with von Willebrand disease (OW19)

February 2025

ONE WALES INTERIM DECISION

Vonicog alfa (Veyvondi®▼) for on-demand treatment of non-surgical and surgical (elective and emergency) bleeding episodes in children aged up to 17 years with von Willebrand disease

Date of original advice: November 2022
Date of review: December 2024

The following One Wales Medicines Assessment Group (OWMAG) recommendation has been noted by the All Wales Medicines Strategy Group (AWMSG) and ratified by Welsh Government

Using the agreed starting and stopping criteria, vonicog alfa (Veyvondi®▼) can be made available within NHS Wales for on-demand treatment of non-surgical and surgical (elective and emergency) bleeding episodes in children aged up to 17 years with von Willebrand disease. Vonicog alfa (Veyvondi®▼) will be available as a second line treatment, given when desmopressin treatment with or without tranexamic acid is ineffective or not indicated.

Vonicog alfa is not licensed to treat this indication and is therefore 'off-label'. Each provider organisation must ensure all internal governance arrangements are completed before this medicine is prescribed.

The risks and benefits of the off-label use of vonicog alfa (Veyvondi®▼) for this indication should be clearly stated and discussed with the patient to allow informed consent.

Providers should consult the relevant guidelines on prescribing unlicensed medicines before any off-label medicines are prescribed.

This advice will be reviewed after 2 years or earlier if new evidence becomes available.

Clinician responsibility
Clinicians will be obliged to collect and monitor patient outcomes. Evidence of clinical outcomes will be taken into consideration when reviewing the One Wales Medicines Assessment Group decision.

Health board responsibility
Health boards will take responsibility for implementing One Wales Medicines Assessment Group decisions and ensuring that a process is in place for monitoring clinical outcomes.

One Wales advice promotes consistency of access across NHS Wales.

Starting and stopping criteria for vonicog alfa for the treatment of surgical (elective and emergency) bleeding episodes in children aged up to 17 years with von Willebrand disease

These criteria are in accordance with the Welsh Health Specialised Services Committee Policy Position PP215: Vonicog alfa for the treatment and prevention of bleeding in people of all ages with von Willebrand disease (October 2023)[1].

Starting criteria:
Vonicog alfa will be routinely commissioned for treatment of haemorrhage and surgical bleeding, and prevention of surgical bleeding, in children aged up to 17 years with a confirmed diagnosis of von Willebrand disease (VWD), in the following circumstances:

- when desmopressin with or without tranexamic acid treatment is ineffective or not indicated (based on UK clinical practice), and
- when von Willebrand Factor (VWF) activity levels are <50 IU/dl OR diagnosis is type 2N VWD, and
- there is no evidence of inhibitors to VWF

Retreatment for the same bleeding episode or surgery should be guided by clinical presentation, considering the half-life of vonicog alfa, with careful monitoring of the necessary laboratory parameters and the patient. Patients, or their carers, should be encouraged to provide their clinical team with information on treatments received for the previous bleeding episode or surgery and related clinical sequelae.

Vonicog alfa should not be prescribed for routine prophylaxis.

Dosage and frequency of administration must be individualised according to clinical judgement and based on the patient´s weight, type and severity of the bleeding episodes/surgical intervention and based on monitoring of appropriate clinical and laboratory measures. Dosing may require adjustment in underweight or overweight patients. Further information about dose calculations can be found in the Summary of Product Characteristics (SmPC)[2].

Stopping criteria:
Treatment with vonicog alfa should be monitored and compared to the effectiveness with previous treatment episodes. Treatment should be discontinued if the following occur:

- reduced or poor control of bleeding with vonicog alfa compared with previous treatment episodes
- unexpected bleeding despite maintenance of therapeutic levels of VWF activity (50 IU/dl or more)
- emergence of adverse effects considered linked to vonicog alfa, such as DVT, hypersensitivity, and infusion-related reactions
- development of anti-VWF neutralising or binding antibodies.

Continuation of treatment:
Healthcare professionals are expected to review a patient's health at regular intervals to ensure they are demonstrating an improvement to their health due to the treatment being given. If no improvement to a patient's health has been recorded then clinical judgement on the continuation of treatment must be made by the treating healthcare professional.

References:

(1) The Welsh Health Specialised Services Committee (WHSSC). PP125 Vonicog alfa for the treatment and prevention of bleeding in people of all ages with von Willebrand disease. October 2023. Available at: https://whssc.nhs.wales/commissioning/whssc-policies/all-policy-documents/vonicog-alfa-for-the-treatment-and-prevention-of-bleeding-in-people-of-all-ages-with-von-willebrand-disease-policy-position-statement-pp2151/. Accessed December 2024.

(2) Takeda UK Ltd. VEYVONDI®. Summary of Product Characteristics. Sep 2024. Available at: https://www.medicines.org.uk/emc/product/11233/smpc#gref. Accessed December 2024.

This is a summary of new evidence available and patient outcome data collected to inform the review

Background: Von Willebrand disease (VWD) is an inherited genetic disorder caused by a missing or defective clotting glycoprotein called von Willebrand factor (VWF), which is essential for normal haemostasis. VWF binds factor VIII (a key clotting protein) and platelets in blood vessel walls, which help form a platelet plug during the clotting process. People with VWD are not able to form this platelet plug, or it takes longer to form.

There is currently no cure for VWD. Clinical practice recommendations for diagnosis, treatment and follow-up were published in 2014 by the United Kingdom Haemophilia Centre Doctors Organisation (UKHCDO). International guidelines produced by the American Society of Haematology (ASH), the International Society on Thrombosis and Haemostasis (ISTH), the National Haemophilia Foundation (NHF), and the World Federation of Haemophilia (WFH) were also published in 2021 to support patients, clinicians, and health care professionals in their decisions about management of VWD. The aim of treatment is to correct the clotting process and reduce the extended bleeding time in people with VWD.

Vonicog alfa is the only recombinant VWF developed for substitution therapy in VWD. It is licensed for use in adults and is commissioned by the NHS Wales Joint Commissioning Committee (JCC). Welsh clinical experts indicated there was an unmet medical need for alternative therapies to the current plasma-derived blood products used in children which have a theoretical risk of transmission of plasma-borne pathogens. This treatment is currently commissioned by JCC for use in children on the basis of the One Wales decision.

The Infected Blood Inquiry report published in May 2024 stated that some people with severe von Willebrand disorder are still being treated with plasma-based factor products; one of the recommendations from the Inquiry is that recombinant coagulation factor products should be offered in place of plasma-derived ones where clinically appropriate and that such treatment decisions should be funded accordingly. This recommendation is particularly pertinent to paediatric patients who are likely to be plasma product naïve.

Current One Wales Decision: Supported for on demand treatment.

Licence status: Off-label use for this licensed medicine.
Vonicog alfa (Veyvondi®) is licenced for the prevention and treatment of haemorrhage or surgical bleeding in adults (age 18 years and older) with von Willebrand disease (VWD), when desmopressin (DDAVP) treatment alone is ineffective or contraindicated. In January 2024, the license was extended to include long-term prophylaxis in adults. [COMMERCIAL IN CONFIDENCE INFORMATION REMOVED].

Guidelines: There have been no relevant updates to existing guidelines identified.

Licensed alternative medicines or Health Technology Assessment advice for alternative medicines: No new medicines or Health Technology Assessment advice reported.

Effectiveness: The repeat literature search found one case study of interest. Tran et al (2023) reported an 8-year-old, Caucasian male diagnosed with mild VWD type 1 with a history of anaphylaxis to Humate-P (plasma-derived VWF blood product) who received vonicog alfa prior to elective orthopaedic surgery. The patient tolerated the recombinant VWF with no notable post infusion-related adverse effects or procedure complications. The patient did require oral aminocaproic acid (an antifibrinolytic) three days post operation due to mild skin bleeding, but he did not require any additional recombinant VWF post operation.

There are currently two active clinical trials:

- A phase 3, prospective, multicentre, uncontrolled, open-label clinical study to determine the efficacy, safety, and tolerability of rVWF with or without rFVIII (Advate®) in the treatment and control of bleeding episodes, the efficacy and safety of rVWF in elective and emergency surgeries, and the pharmacokinetics of rVWF in children diagnosed with severe von Willebrand disease (NCT02932618). This study is still recruiting but has a primary completion date January 2025.
- A phase 3b, prospective, open-label, uncontrolled, multicentre study on long-term safety and efficacy of rVWF in paediatric and adult subjects with severe von Willebrand disease (NCT03879135). This study is due to complete in March 2025.

There is a pending clinical trial which will evaluate the effectiveness of prophylaxis with rVWF in children which is due to complete in February 2027 (NCT05582993). Although not pertinent to the indication in this report, this trial may provide some useful safety data for the use of rWF in paediatric patients.

Safety: Outcome data provided by the Cardiff Haemophilia Centre report no adverse events, either at the time of infusion or in the recovery period. No other relevant safety analyses were identified in the repeat literature search.

Cost-effectiveness: No relevant cost-effectiveness analyses were identified in the repeat literature search.

Budget impact: There have been six paediatric patients in Wales treated with vonicog alfa, each for a single bleeding event, between August 2023 and October 2024. The dose given ranged from 650 IU to 2600 IU with the number of doses per patient ranging from 1 to 13. [CONFIDENTIAL DATA REMOVED]. The total cost associated with the use of vonicog alfa over the 17-month period reported is [CONFIDENTIAL DATA REMOVED]. This compares favourably with that estimated for the time period covered by the previous review which was [CONFIDENTIAL DATA REMOVED] over 18 months and with the original yearly estimate of [CONFIDENTIAL DATA REMOVED]. None of these estimates include VAT.

In the original budget impact, it was assumed that one dose of vonicog alfa would be used in a population of twenty children (20 doses), assuming some vial wastage. To take account of the varying ages of the population a mid-point age was used. Calculations were based on the average weight of a 9-year old child receiving a vonicog alfa dose of 46.5 IU/kg and a rFVIII dose of 33.6 IU/kg. As was noted in the previous review, actual usage data shows that fewer children than predicted receive treatment with vonicog alfa per year but in general, more than one dose is required

per bleeding episode (mean number of doses 4.5, range 1-13). Additionally, concomitant rVIII is not required in many patients. Despite quite differing results in terms of doses used and patient uptake, the budget impact was lower in Year 2 when compared to the original estimates. AWTTC will continue to monitor patient uptake as part of ongoing reviews.

Impact on health and social care services: Minimal.

Patient outcome data: Data have been received for six patients (age range 3 -17 years) in Wales each treated with vonicog alfa for a single bleeding event. All patients were treated at the Cardiff Haemophilia Centre which treats paediatric patients from all health board areas apart from Betsi Cadwaladr UHB in North Wales. No patient outcome data has been received for patient's resident in North Wales and who would generally receive this specialist treatment at Alder Hey Children's Hospital in Liverpool.

[CONFIDENTIAL DATA REMOVED]. Resolution of bleeding was reported for all patients treated with vonicog alfa with no requirement to escalate to third-line treatments. No post-surgical complications were reported.

Evaluation of evidence

No significant new evidence has been published which challenges the original recommendation. Outcome data provided suggest that this treatment has been well tolerated and associated with resolution of symptoms. The number of doses used is higher than originally predicted. However, the overall budget impact is lower than the original estimate due to the number of patients treated. AWTTC will continue to monitor this as part of the review process and report back to OWMAG. AWTTC recommends continuing access in Wales to vonicog alfa for the on-demand treatment of non-surgical and surgical (elective and emergency) bleeding episodes in children aged up to 17 years with von Willebrand disease.

Next review date: December 2026

References: A full reference list is available on request