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)

December 2023

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: November 2023

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 12 months 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 November 2023.

(2) Takeda UK Ltd. VEYVONDI®. Summary of Product Characteristics. Jun 2023. Available at: https://www.medicines.org.uk/emc/product/11233/smpc#gref. Accessed November 2023.

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). 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 Welsh Health Specialised Services Committee (WHSSC). 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 WHSSC for use in children on the basis of the One Wales decision.

Current One Wales Decision: Supported for on demand treatment.

Licence status: Off-label use for this licensed medicine.

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: A repeat literature search conducted by AWTTC identified one poster presented at the 16th Annual Congress of European Association for Haemophilia and Allied Disorders. This information was produced by the Cardiff Haemophilia Centre, the data from which has been reported separately to AWTTC and is provided in the appendix.

Safety: Outcome data provided by the Cardiff Haemophilia Centre report no adverse events, either at the time of infusion or in the recovery period. It was however noted that more data for this population is required. An incidence of [CONFIDENTIAL DATA REMOVED]. 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: In the original evidence summary it was estimated that 20 paediatric patients per year would be eligible for on demand treatment with vonicog alfa. In fact, there have been six patients in Wales treated with vonicog alfa for 12 bleeding events between April 2022 and September 2023. Some of these cases would have

been prior to the availability of vonicog alfa through the One Wales decision in November 2022; treatment before this would have been initiated following agreement through the Individual Patient Funding Request (IPFR) process. However, all these bleeding events have been considered as part of this review in order to make a comparison with the estimated annual spend for vonicog alfa in this patient group as detailed in the original One Wales assessment report.

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 46.5IU/kg and a recombinant factor VIII (rFVIII) dose of 33.6IU/kg. These were the median dosages per bleed reported by Gill et al. This resulted in an estimated yearly cost of [CONFIDENTIAL DATA REMOVED] for the use of vonicog alfa in the paediatric population.

Whilst our original estimates suggested a single dose may be adequate, 10 of the 12 bleeding episodes, experienced by the six paediatric patients since April 2022, required at least two doses of vonicog alfa with some requiring up to four. Doses given ranged from 35-75 units/kg. In total, 22 doses of vonicog alfa were received for 10 of the bleeding episodes reported. [CONFIDENTIAL DATA REMOVED].

The contract price of rFVIII has dropped significantly since that reported in the original budget impact. Furthermore, not all bleeding events treated (8 out of 12) required concomitant rFVIII; representing a cost saving. The total costs associated with the administration of vonicog alfa for the 12 bleeding episodes reported has been estimated as [CONFIDENTIAL DATA REMOVED]. This is an estimate as only the ages of the treated children were reported. The number of vials of vonicog alfa and rFVIII required were calculated using average weights as given in the BNFC. Overall, this compares favourably with the original estimate which, when extrapolated over 18 months, would be [CONFIDENTIAL DATA REMOVED].

Despite quite differing results in terms of doses used and patient uptake, the budget impact was lower in year one 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 in Wales treated with vonicog alfa for 12 bleeding events (see appendix). 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 have been received for patients resident in North Wales and who would generally receive this specialist treatment at Alder Hey Children's Hospital in Liverpool.

Eight of the 12 bleeding episodes were caused by non-surgical events: [CONFIDENTIAL DATA REMOVED]. Resolution of bleeding was reported for all patients treated with vonicog alfa with no requirement to escalate to third-line treatments. Clinicians from the Cardiff Haemophilia Centre state that vonicog alfa appears to be as efficacious for the on-demand treatment of non-surgical and surgical (elective and emergency) bleeding episodes in the paediatric population as it is in the licensed adult population and that it is now standard practice to discuss the

off-label use of vonicog alfa with paediatric patients and their carers pre-emptively in clinic.

None of the children treated had any previous exposure to plasma-derived products and the use of vonicog alfa instead of licensed plasma-derived VWF means these patients remain free from the theoretical risk of blood-borne pathogen transmission. The Cardiff Haemophilia Centre have plans to submit these data for publication in a peer-reviewed journal in due course.

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 age and 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 severe von Willebrand disease.

Next review date: November 2024

References: A full reference list is available on request.

Appendix: [CONFIDENTIAL DATA REMOVED]

This document includes evidence published since the last review or full assessment of this medicine for the indication under consideration. It does not replace the original full evidence status report. Any previous reviews and the original full evidence status report are available on request by email to AWTTC@wales.nhs.uk.

Care has been taken to ensure the information is accurate and complete at the time of publication. However, the All Wales Therapeutics and Toxicology Centre (AWTTC) do not make any guarantees to that effect. The information in this document is subject to review and may be updated or withdrawn at any time. AWTTC accept no liability in association with the use of its content. An Equality and Health Impact Assessment (EHIA) has been completed in relation to the One Wales policy and this found there to be a positive impact. Key actions have been identified and these can be found in the One Wales Policy EHIA document.

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