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)

November 2022

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 advice: November 2022

The following One Wales Medicines Assessment Group (OWMAG) recommendation has been endorsed by health board Chief Executives.

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.

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.

This advice will be reviewed after 12 months or earlier if new evidence becomes available.

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 adapted from the Welsh Health Specialised Services Committee Policy Position PP215: Vonicog alfa for the treatment and prevention of bleeding in adults with von Willebrand disease (May 2021)[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 adults with von Willebrand disease 2021. Available at: https://whssc.nhs.wales/commissioning/whssc-policies/all-policy-documents/vonicog-alfa-for-the-treatment-and-prevention-of-bleeding-in-adults-with-von-willebrand-disease-policy-position-statement-pp215-may-2021/ . Accessed Oct 2022.

(2) Takeda UK Ltd. VEYVONDI®. Summary of Product Characteristics. Aug 2022. Available at: https://www.medicines.org.uk/emc/product/11233/smpc#gref. Accessed Oct 2022.

One Wales Medicine Assessment Group summary of decision rationale

Medicine: **vonicog alfa (Veyvondi®▼)**
Indication**: vonicog alfa (Veyvondi®▼) for the for 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**
Meeting date: **26 September 2022**

Note: The clinical expert in attendance requested that the indication be amended to align with the WHSSC commissioning criteria of vonicog alfa (Veyvondi) in adults. Therefore, the indication has been revised to also include the on-demand treatment of non-surgical bleeding episodes in children.

As the ESR provides evidence to support use in both surgical and non-surgical bleeding episodes, OWMAG agreed that a recommendation could be made at this meeting for this revised indication. OWMAG requested that the indication in the ESR was updated and the budget impact re-calculated to reflect the small expected increase in predicted patient numbers.The OWMAG discussions and opinions detailed below refer to the revised indication.

Criteria	OWMAG opinion
Clinical effectiveness	OWMAG notes that data in children are lacking. The evidence of clinical efficacy for vonicog alfa comes mainly from two clinical trials in the adult population. Both trials concluded vonicog alfa is safe and haemostatically effective in adults with severe von Willebrand disease in a variety of clinical bleeding presentations. OWMAG notes that two phase III clinical trials of vonicog alfa are underway in the paediatric population. OWMAG considers that the evidence provided demonstrated clinical effectiveness in adults and that it is reasonable to expect that the therapeutic response to vonicog alfa in children would be similar. The clinical expert in attendance confirmed that this is expected to be the case. OWMAG notes that safety data in children are lacking. The known safety profile for vonicog alfa comes mainly from the same two clinical trials in the adult population as described above. Most of the treatment-related adverse events reported in the adult studies were mild to moderate in severity.
Cost-effectiveness	OWMAG notes that no cost-effectiveness evidence is available for either the adult or paediatric populations.
Budget impact	OWMAG acknowledges that vonicog alfa is a direct replacement for plasma-derived VWF and the benefit of removing the risk of blood-borne pathogen transmission for the paediatric population outweighs the small predicted increased cost for vonicog alfa per patient per treatment. OWMAG note that a large proportion of the increased cost is due to use of concomitant rFVIII which may not be required for some patients. OWMAG notes that vonicog alfa is available to NHS Wales at a confidential discounted

	price. OWMAG notes that vonicog alfa is a second-line treatment option when desmopressin treatment with or without tranexamic acid is ineffective or not indicated.
Other factors	The clinical expert in attendance requested that the indication be extended to include on-demand treatment of non-surgical bleeding episodes in children. OWMAG notes the rationale for the preferred use of unlicensed vonicog alfa in children over the licensed plasma-derived alternative product in that the theoretical risk of blood-borne pathogen transmission is removed.
Final recommendation	OWMAG recommends vonicog alfa (Veyvondi®▼) 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. This recommendation is subject to the development of appropriate start/stop criteria.
Summary of rationale	There is evidence to support vonicog alfa as an effective treatment option for bleeding episodes in adults with severe von Willebrand disease. Although data specific to the paediatric population is currently lacking, it would seem reasonable to expect that both the therapeutic response to and the safety profile of vonicog alfa in children would be similar to that in adults. OWMAG considers that the removal of the theoretical risk of blood-borne pathogen transmission is the primary consideration in supporting the use of vonicog alfa in the paediatric population

The information in this document is intended to help healthcare providers make an informed decision. This document should not be used as a substitute for professional medical advice. 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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