GIG CYMRU NHS WALES

Pwyllgor Gwasanaethau Iechyd Arbenigol Cymru (PGIAC)

Welsh Health Specialised Services Committee (WHSSC)

Specialised Services
Policy Position Statement PP215

Vonicog alfa for the treatment and prevention of bleeding in people of all ages with von Willebrand disease

October 2023

Version 2.0

PARCH - RESPECT

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Description	NHS Wales commission this specialised service in accordance with the criteria described in this policy
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Contents

Policy Statement

Welsh Health Specialised Services Committee (WHSSC) will commission vonicog alfa for people of all ages with von Willebrand disease in accordance with the criteria outlined in this document.

In creating this document WHSSC has reviewed the relevant guidance issued by NHS England[1] and the interim One Wales decision issued by AWMSG[2] and has concluded that vonicog alfa should be made available.

Welsh Language

WHSSC is committed to treating the English and Welsh languages on the basis of equality, and endeavour to ensure commissioned services meet the requirements of the legislative framework for Welsh Language, including the Welsh Language Act (1993), the Welsh Language (Wales) Measure 2011 and the Welsh Language Standards (No.7) Regulations 2018.

Where a service is provided in a private facility or in a hospital outside of Wales, the provisions of the Welsh language standards do not directly apply but in recognition of its importance to the patient experience, the referring health board should ensure that wherever possible patients have access to their preferred language.

In order to facilitate this, WHSSC is committed to working closely with providers to ensure that in the absence of a Welsh speaker, written information will be offered and people have access to either a translator or 'Language-line' if requested. Where possible, links to local teams should be maintained during the period of care.

Decarbonisation

WHSSC is committed to taking assertive action to reducing the carbon footprint through mindful commissioning activities. Where possible and taking into account each individual patient's needs, services are provided closer to home, including via digital and virtual access, with a delivery chain for service provision and associated capital that reflects the WHSSC commitment.

Disclaimer

WHSSC assumes that healthcare professionals will use their clinical judgment, knowledge and expertise when deciding whether it is appropriate to apply this policy position statement.

[1] https://www.england.nhs.uk/wp-content/uploads/2020/09/1709-cc-policy-vonicog-alfa-for-von-willebrand-disease.pdf
[2] https://awttc.nhs.wales/files/one-wales/one-wales-interim-decision-with-decision-rationale-and-start-stop-criteria-vonicog-alfa-for-children-with-vwd-ow19-2022/

This policy may not be clinically appropriate for use in all situations and does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

WHSSC disclaims any responsibility for damages arising out of the use or non-use of this policy position statement.

1. Introduction

This Policy Position Statement has been developed for the planning and delivery of vonicog alfa for people resident in Wales. This service will only be commissioned by the Welsh Health Specialised Services Committee (WHSSC) and applies to residents of all seven Health Boards in Wales.

1.1 Plain language summary

People with von Willebrand disease (VWD) have a low amount of a missing protein called von Willebrand factor (VWF) in their blood, or this protein doesn't work very well. This means that people with VWD have difficulty forming a blood clot (which is needed to stop bleeding when it occurs), and as a result, they bleed more after events such as injury, childbirth, or during surgery. Symptoms can range from very mild and barely noticeable to frequent and severe, and can include nosebleeds, bleeding from the gums, easy bruising, and heavy menstrual bleeding. VWD has 3 main types (known as VWD types 1, 2, and 3), with differing levels of severity.[3]

1.2 Aims and Objectives

This Policy Position Statement aims to define the commissioning position of WHSSC on the use of vonicog alfa for people with von Willebrand disease.

The objectives of this policy are to:

- ensure commissioning for the use of vonicog alfa is evidence based
- ensure equitable access to vonicog alfa
- define criteria for people with von Willebrand disease to access treatment
- improve outcomes for people with von Willebrand disease.

1.3 Epidemiology

Based on the Bleeding Disorder Statistics for Wales from April 2021 to March 2022 Report from the UK National Haemophilia Database, it is estimated that 487 people have von Willebrand disease in Wales, 90 of whom were <18 years of age. A total of 44 people with von Willebrand disease were treated with concentrates during the same time period, 9 of whom were treated with Veyvondi®▼ (vonicog alfa). The eligible patient population for vonicog alfa in Wales is considered equivalent to people with all types of VWD who are currently treated with plasma concentrates but excluding those using the concentrates for prophylaxis. This is estimated to be approximately 54 people[4].

[3] NHS choices: von Willebrand disease

[4] This estimate is derived from the number provided in the previous iteration of this policy (34) plus the estimate used by the AWTTC in their evidence report (20 patients).

1.4 Current Treatment

Treatment aims to correct the clotting process and reduce the extended bleeding time in people with VWD. Treatments for stopping and preventing bleeds in people with VWD include tranexamic acid, desmopressin, or products made from human blood containing either VWF alone or VWF with another protein that helps with blood clots (known as factor 8).

Choice of treatment depends on type and severity of the condition and bleed. In some people with VWD who have some working VWF, desmopressin works by temporarily boosting their own factor 8 and VWF. It is used for treating bleeding complications or given before surgery for preventing bleeding. Tranexamic acid works by stopping the breakdown of clots and can be used with other treatments. It is used for treating minor bleeding or used before surgery. Blood-derived products are made using human blood and commonly contain both VWF and factor 8 to help the blood to clot. They are used for preventing and treating bleeding in major surgery or for treating serious bleeding episodes.

Plasma-derived products are effective and have an excellent safety record, however there are disadvantages compared to artificially made alternatives which are not dependent on donor availability. Blood derived products can also vary in their effectiveness to help clotting due to natural differences in the VWF protein found in human blood. Plasma-derived blood products used in the UK have an excellent recent safety history though there remains a theoretical risk of plasma-borne pathogen transmission.

1.5 Proposed Treatment

Vonicog alfa works in the body in the same way as von Willebrand factor made by the body itself, by replacing the protein needed to stop bleeding that is missing or not working. It has been artificially made rather than taking it from plasma. Vonicog alfa may be preferred over products taken from plasma because it is less likely to have the problems highlighted above, and, as factor 8 does not need to be given with every dose of vonicog alfa, it avoids the risk of factor 8 building up in the body (a risk factor for clots). It is administered as an intravenous infusion for treating on demand bleeding episodes and for preventing and treating bleeding during surgery. Vonicog alfa is the only recombinant human VWF for people with VWD.

Vonicog alfa is currently licensed only for adults (age 18+ years) and only for short-term episodic use (such as 'on demand' to treat bleeding episodes and to prevent and treat bleeding during surgery).

The All Wales Medicines Strategy Group (AWMSG) endorsed a One Wales interim decision in November 2022 to make vonicog alfa available 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[5]. This advice will be reviewed after 12 months or earlier if new evidence becomes available.

1.6 Off-label use

Vonicog alfa is not licenced to treat this indication in children (aged 0-17) and is therefore "off –label". A clinician considering prescribing a medication outside of the terms of a product licence (off-label) should do so in accordance with the Medicines and Healthcare Products Agency (MHRA)[6] and the General Medical Council (GMC) guidance[7] which applies throughout the UK.

The risk and benefits of off-label use of vonicog alfa should be clearly stated and discussed with the patient to enable informed consent.

Should clinicians consider the treatment appropriate for their patients and they have followed local medicines governance arrangements for off-label use, WHSSC will meet the cost under the criteria set out in 2.1.

1.7 What NHS Wales has decided

WHSSC has carefully reviewed the relevant guidance issued by NHS England[8] and the interim One Wales decision issued by AWMSG[9]. We have concluded that vonicog alfa, should be made available to treat people with von Willebrand disease within the criteria set out in section 2.1.

[5] https://awttc.nhs.wales/files/one-wales/one-wales-interim-decision-with-decision-rationale-and-start-stop-criteria-vonicog-alfa-for-children-with-vwd-ow19-2022/
[6] https://www.gov.uk/drug-safety-update/off-label-or-unlicensed-use-of-medicines-prescribers-responsibilities
[7] https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/good-practice-in-prescribing-and-managing-medicines-and-devices/prescribing-unlicensed-medicines
[8] https://www.england.nhs.uk/wp-content/uploads/2020/09/1709-cc-policy-vonicog-alfa-for-von-willebrand-disease.pdf
[9] https://awttc.nhs.wales/files/one-wales/one-wales-interim-decision-with-decision-rationale-and-start-stop-criteria-vonicog-alfa-for-children-with-vwd-ow19-2022/

2. Criteria for Commissioning

The Welsh Health Specialised Services Committee approve funding of vonicog alfa for people with von Willebrand disease, in-line with the criteria identified in the policy.

2.1 Inclusion Criteria

Vonicog alfa will be routinely commissioned for treatment of haemorrhage and surgical bleeding, and prevention of surgical bleeding, in people with a confirmed diagnosis of 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 VWF activity levels are <50 IU/dl[10] 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, taking into account 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. This is most easily achieved through the use of a secure therapy recording digital interface, for example Haemtrack.

2.2 Exclusion Criteria

Vonicog alfa will not be routinely commissioned for:

- routine prophylaxis in patients of any age.

2.3 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.

[10] see British Society of Haematology guidelines on the diagnosis and management of von Willebrand disease 2014

2.4 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.

2.5 Acceptance Criteria

The service outlined in this policy position is for patients ordinarily resident in Wales, or otherwise the commissioning responsibility of the NHS in Wales. This excludes patients who whilst resident in Wales, are registered with a GP practice in England, but includes patients resident in England who are registered with a GP Practice in Wales.

2.6 Patient Pathway (Annex i)

The choice of treatment for treating bleeding episodes, and treating and preventing bleeding during surgery, will be based on the efficacy of the product to control the severity of bleed, and the type and location of surgery, taking into account clinical evaluation and shared decision making with the patient where appropriate. The pathway shown in Annex i outlines that vonicog alfa will be available as a second line treatment, given when desmopressin and tranexamic acid treatment are ineffective or not indicated.

Plasma derived VWF is current standard of care at second line, and it will remain a treatment choice at this point in the pathway. Historically in the UK, recombinant factor concentrates (when available) have been used in preference to plasma derived products on account of historical problems with transfusion transmitted infection (as noted by Gill et al. 2015). Although the safety record of modern plasma derived factor concentrates is excellent, it is anticipated that the principle of 'recombinant for all' will be an important consideration in choice of product. There is currently no evidence from clinical studies that vonicog alfa has any other advantage over plasma derived VWF concentrate. When more than one product is deemed suitable, the product with the lowest overall acquisition cost to control a bleed should be chosen (taking into account the cost of co-administration with recombinant factor 8 [rFVIII] where required).

2.7 Exceptions

If the patient does not meet the criteria for treatment as outlined in this policy, an Individual Patient Funding Request (IPFR) can be submitted for consideration in line with the All Wales Policy: Making Decisions on Individual Patient Funding Requests. The request will then be considered by the All Wales IPFR Panel.

If the patient wishes to be referred to a provider outside of the agreed pathway, an IPFR should be submitted.

Further information on making IPFR requests can be found at: Welsh Health Specialised Services Committee (WHSSC) | Individual Patient Funding Requests

2.8 Clinical Outcome and Quality Measures

The Provider must work to written quality standards and provide monitoring information to the lead commissioner.

The centre must enable the patient's, carer's and advocate's informed participation and to be able to demonstrate this. Provision should be made for patients with communication difficulties.

Specialised centres will be required to ensure that processes are in place to track decisions to treat and evidence of effectiveness. Patients with Von Willebrand disease should be registered in the National Haemophilia Database (NHD) and any products used to manage bleeding episodes in VWD should be recorded within the NHD. Centres may use software systems to track and audit use of vonicog alfa, in order to ensure it is administered according to the Criteria for Commissioning.

2.9 Responsibilities

Treatment with vonicog alfa should be under the supervision of a physician experienced in the treatment of haemostatic disorders.

Referrers should:

- inform the patient that this treatment is not routinely funded outside the criteria in this policy, and
- refer via the agreed pathway.

Clinicians considering treatment should:

- discuss all the alternative treatment with the patient
- advise the patient of any side effects and risks of the potential treatment
- inform the patient that treatment is not routinely funded outside of the criteria in the policy, and
- confirm that there is contractual agreement with WHSSC for the treatment
- collect and monitor patient outcomes
- state and discuss the risks and benefits of the off-label use of vonicog alfa (Veyvondi®▼) for this indication with the patient and/or with the patient's carer to allow informed consent in the case of use in children aged up to 17 years.

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.

In all other circumstances an IPFR must be submitted.

2.10 Designated Providers

The following centres provide this treatment:

University Hospital of Wales
Health Park Way
Cardiff
CF14 4XW

Alderhey Children's Hospital
East Prescot Road
Liverpool
L14 5AB

The Roald Dahl Haemostasis and Thrombosis Centre
Royal Liverpool & Broadgreen University Hospital Trust NHS
Prescott Street
Liverpool
L7 8XP

2.11 Blueteq and reimbursement

Vonicog alfa will only be funded for patients registered via the Blueteq system and where an appropriately constructed MDT has approved its use within highly specialised haematology centres.

Where the patient meets the criteria in this policy and the referral is received by an agreed centre, a Blueteq form should be completed for approval. For further information on accessing and completing the Blueteq form please contact WHSSC using the following e-mail address: WHSSC.blueteq@wales.nhs.uk

If a non-contracted provider wishes to treat a patient that meets the criteria they should contact WHSSC (e-mail: WHSSC.IPC@Wales.nhs.uk). They will be asked to demonstrate they have an appropriate MDT in place.

Vonicog alfa is administered by intravenous infusion. 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[11].

The list price of vonicog alfa is £598.00 per 650IU vial and £1,196.00 per 1300IU vial (excluding VAT).

[11] https://www.medicines.org.uk/emc/product/11233/smpc

3. Documents which have informed this policy

The following documents have been used to inform this policy:

- **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 (OW19), November 2022

- **NHS England policies**
  - Vonicog alfa for the treatment and prevention of bleeding in adults with von Willebrand disease, 200801P [1709], January 2021

This document should be read in conjunction with the following documents:

- **NHS Wales**
  - All Wales Policy: Making Decisions in Individual Patient Funding requests (IPFR).

4. Date of Review

This document will be reviewed when information is received which indicates that the policy requires revision.

5. Putting Things Right

5.1 Raising a Concern

Whilst every effort has been made to ensure that decisions made under this policy are robust and appropriate for the patient group, it is acknowledged that there may be occasions when the patient or their representative are not happy with decisions made or the treatment provided.

The patient or their representative should be guided by the clinician, or the member of NHS staff with whom the concern is raised, to the appropriate arrangements for management of their concern.

If a patient or their representative is unhappy with the care provided during the treatment or the clinical decision to withdraw treatment provided under this policy, the patient and/or their representative should be guided to the LHB for NHS Putting Things Right. For services provided outside NHS Wales the patient or their representative should be guided to the NHS Trust Concerns Procedure, with a copy of the concern being sent to WHSSC.

5.2 Individual Patient Funding Request (IPFR)

If the patient does not meet the criteria for treatment as outlined in this policy, an Individual Patient Funding Request (IPFR) can be submitted for consideration in line with the All Wales Policy: Making Decisions on Individual Patient Funding Requests. The request will then be considered by the All Wales IPFR Panel.

If an IPFR is declined by the Panel, a patient and/or their NHS clinician has the right to request information about how the decision was reached. If the patient and their NHS clinician feel the process has not been followed in accordance with this policy, arrangements can be made for an independent review of the process to be undertaken by the patient's Local Health Board. The ground(s) for the review, which are detailed in the All Wales Policy: Making Decisions on Individual Patient Funding Requests (IPFR), must be clearly stated.

If the patient wishes to be referred to a provider outside of the agreed pathway, an IPFR should be submitted.

Further information on making IPFR requests can be found at: Welsh Health Specialised Services Committee (WHSSC) | Individual Patient Funding Requests

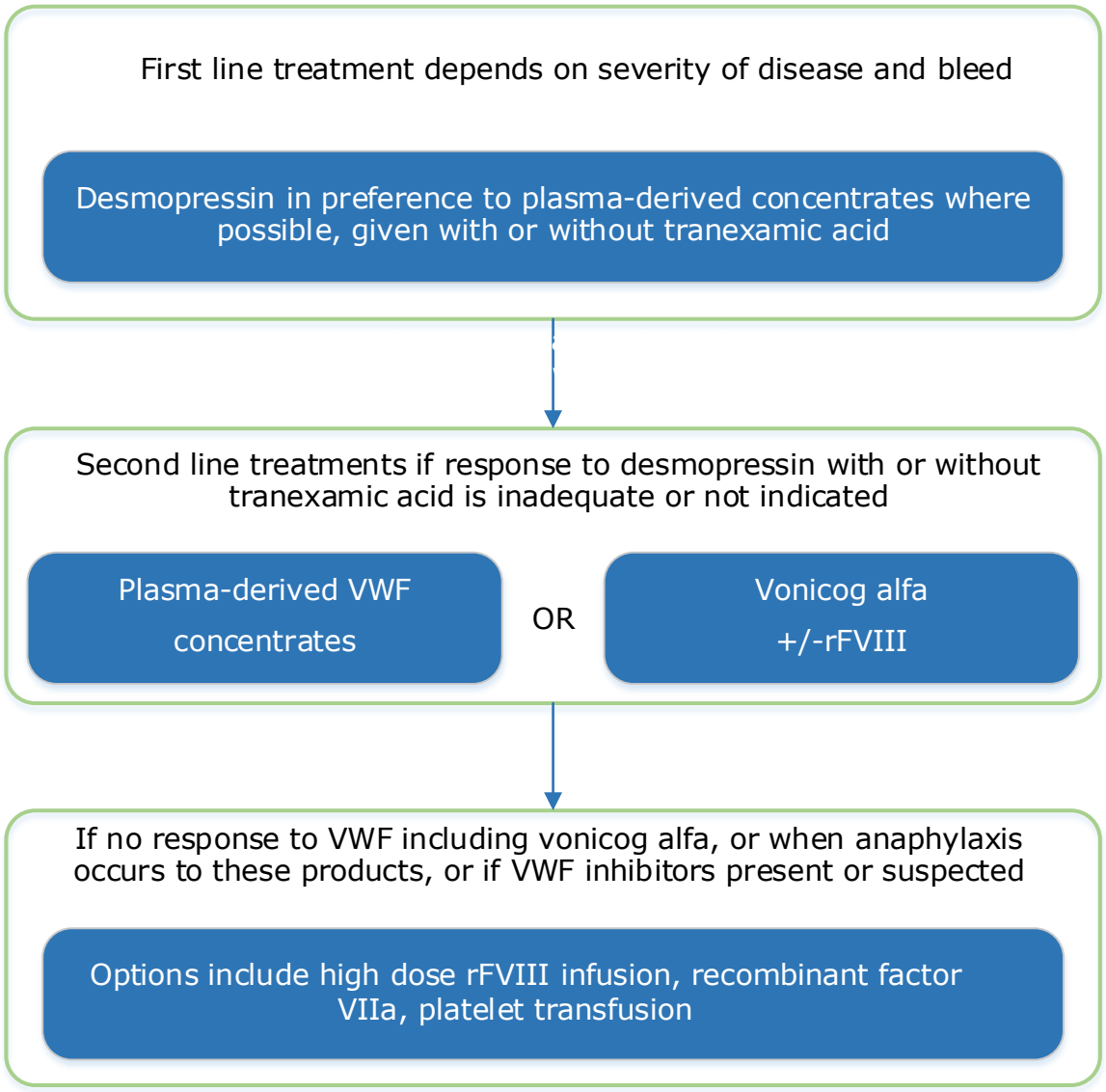
6. Equality Impact and Assessment

The Equality Impact Assessment (EQIA) process has been developed to help promote fair and equal treatment in the delivery of health services. It aims to enable Welsh Health Specialised Services Committee to identify and eliminate detrimental treatment caused by the adverse impact of health service policies upon groups and individuals for reasons of race, gender re-assignment, disability, sex, sexual orientation, age, religion and belief, marriage and civil partnership, pregnancy and maternity and language (Welsh).

This policy has been subjected to an Equality Impact Assessment.

The Assessment demonstrates the policy is robust and there is no potential for discrimination or adverse impact. All opportunities to promote equality have been taken.

Annex i Patient Pathway



Annex ii Codes

Code Category	Code	Description
ICD-10	D68	Von Willebrand's Disease

Annex iii Abbreviations and Glossary

Abbreviations

AWMSG All Wales Medicines Strategy Group

IPFR Individual Patient Funding Request

WHSSC Welsh Health Specialised Services

Glossary

All Wales Medicines Strategy Group (AWMSG)
AWMSG advises Welsh Government on a range of strategic developments on the prescribing of medicines. They also produce guidance to support the best use of medicines to help patients in Wales be healthier and better-informed.

Factor 8 (or factor VIII, FVIII)
A blood clotting protein.

Individual Patient Funding Request (IPFR)
An IPFR is a request to Welsh Health Specialised Services Committee (WHSSC) to fund an intervention, device or treatment for patients that fall outside the range of services and treatments routinely provided across Wales.

Plasma-derived products
Derived from human plasma and include von Willebrand factor in combination with factor 8.

Recombinant factor 8 (rFVIII)
FVIII made in a cell line using recombinant DNA techniques (therefore not from human plasma).

Recombinant von Willebrand factor
VWF made in a cell line using recombinant DNA techniques (therefore not from human plasma).

Von Willebrand factor
This is a large protein essential for normal haemostasis. It binds to damaged blood vessel walls and captures platelets, to form a platelet plug which is the first step in stopping bleeding. It also binds FVIII and prolongs its survival in the circulation.

Von Willebrand disease
The disorder due to a deficiency or functional abnormality of von Willebrand factor.

Welsh Health Specialised Services Committee (WHSSC)
WHSSC is a joint committee of the seven local health boards in Wales. The purpose of WHSSC is to ensure that the population of Wales has fair and equitable access to the full range of Specialised Services and Tertiary Services. WHSSC ensures that specialised services are commissioned from

providers that have the appropriate experience and expertise. They ensure that these providers are able to provide a robust, high quality and sustainable services, which are safe for patients and are cost effective for NHS Wales.