

A guide to VEYVONDI dosing on demand and for elective surgery



This document is intended for UK healthcare professionals who treat adults with von Willebrand disease. This document is not intended to replace the Summary of Product Characteristics (please refer to section 4.2 for full information).

VEYVONDI is licensed for the treatment of haemorrhage and in surgery as follows: VEYVONDI is indicated in adults (age 18 and older) with von Willebrand disease (VWD), when desmopressin (DDAVP) treatment alone is ineffective or not indicated for the:

- Treatment of haemorrhage and surgical bleeding
- Prevention of surgical bleeding

VEYVONDI should not be used in the treatment of Haemophilia A.¹

Treatment of VWD should be supervised by a physician experienced in the treatment of haemostatic disorders.¹

On-demand treatment of bleeding episodes¹

STEP 1 INITIAL DOSE OF VEYVONDI	
<p>VEYVONDI dose (IU) = dose (IU/kg) x weight (kg) Infusion rate up to a maximum of 4 ml/min Patient should be observed for any immediate reaction Replacement levels of VWF:RCo >0.6 IU/ml (60%) and FVIII:C >0.4 IU/ml (40%) should be achieved</p>	
<p>MINOR HAEMORRHAGE VEYVONDI 40–50 IU/kg BODY WEIGHT e.g. epistaxis, oral bleeding, menorrhagia</p>	<p>MAJOR HAEMORRHAGE* VEYVONDI 50–80 IU/kg BODY WEIGHT e.g. severe or refractory epistaxis, menorrhagia, gastrointestinal bleeding, central nervous system trauma, haemarthrosis, or traumatic haemorrhage</p>

STEP 2 CHECK FVIII:C LEVELS	
<p>Are FVIII:C Levels <40%? or unknown, or does the situation require a rapid correction of haemostasis, such as treatment of an acute haemorrhage, severe trauma, or emergency surgery?</p>	
<p>NO The physician may decide to omit the co-administration of rFVIII[†] at the first infusion with VEYVONDI</p>	<p>YES The complete dose of VEYVONDI should be administered followed by rFVIII[†] within 10 minutes</p>
<p>The rFVIII[†] dose should be calculated according to the difference between the patient's baseline plasma FVIII:C level, and the desired peak FVIII:C level to achieve an appropriate plasma FVIII:C level based on the approximate mean recovery of 0.02 (IU/ml)/(IU/kg)</p>	

STEP 3 SUBSEQUENT VEYVONDI INFUSIONS	
<p>MINOR HAEMORRHAGE VEYVONDI 40–50 IU/kg every 8–24 hours (or as long as deemed clinically necessary)</p>	<p>MAJOR HAEMORRHAGE* VEYVONDI 40–60 IU/kg every 8–24 hours for approximately 2–3 days (or as long as deemed clinically necessary)</p> <ul style="list-style-type: none"> • In major bleeding episodes, maintain trough levels of VWF:RCo >50% for as long as deemed necessary
<p>Once VWF has been replaced, endogenous FVIII levels will remain normal or near normal as long as VEYVONDI continues to be administered**</p> <ul style="list-style-type: none"> • In case of major bleeding events or major surgeries requiring repeated, frequent infusions, monitoring of FVIII:C levels is recommended, to decide if rFVIII is required for subsequent infusions to avoid excessive rise of FVIII:C 	

*A bleed could be considered major if red blood cell transfusion is either required or potentially indicated, or if bleeding occurs in a critical anatomical site (e.g. intracranial or gastrointestinal haemorrhage).

**Based on experience from clinical studies.¹

[†]No pure/recombinant FVIII products are licensed in VWD.

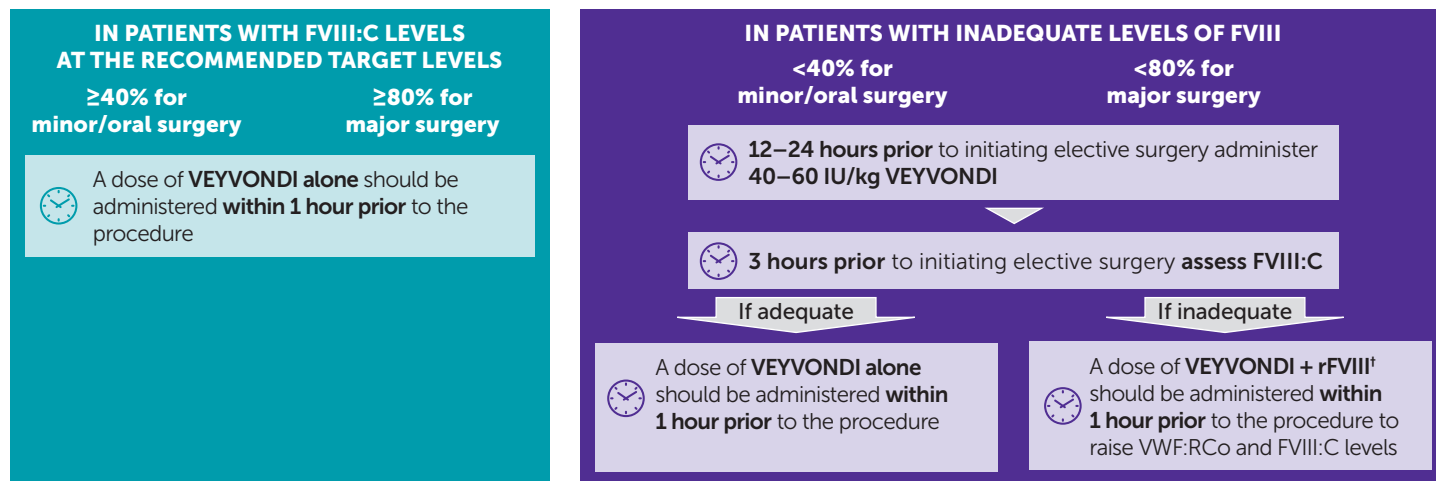
VWF= von Willebrand factor, FVIII= factor FVIII, FVIII:C= FVIII activity, rFVIII= recombinant FVIII, VWF:RCo= VWF ristocetin cofactor activity

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Prevention of bleeding/haemorrhage and treatment in elective surgery¹

STEP 1: Prior to elective surgery



[†]Octocog alfa and ruriocog alfa pegol are not indicated in von Willebrand disease

Recommended target peak plasma levels of VWF:RCo and FVIII:C to be achieved prior to surgery for the prevention of excessive bleeding during and after surgery

Target peak plasma levels		VWF:RCo	FVIII:C*
Type of surgery	Minor	50–60%	40–50%
	Major	100%	80–100%

*Additional rFVIII[†] may be required to attain the recommended FVIII:C target peak plasma levels. Dosing should be based on the approximate mean incremental recovery (0.02 IU/ml per IU/kg).

Calculating VEYVONDI dose within 1 hour of procedure based on recommended target peak plasma levels

[Target peak plasma VWF:RCo – baseline plasma VWF:RCo] x body weight (kg) divided by incremental recovery (IR)
If IR is not available, assume an IR of 0.02 IU/ml per IU/kg.

STEP 2: During and after surgery

- Monitor VWF:RCo and FVIII:C plasma levels
- Intraoperative and postoperative substitution regimen should be individualised according to PK results, intensity and duration of haemostatic challenge and your hospital's standard of care
- In general, frequency of postoperative substitution with VEYVONDI should range from twice a day to every 48 hours

Recommended target trough plasma levels of VWF:RCo and FVIII:C and minimum duration of treatment for subsequent maintenance doses for the prevention of excessive bleeding after surgery

TYPE OF SURGERY	TARGET TROUGH PLASMA LEVEL				MINIMUM DURATION OF TREATMENT	FREQUENCY OF DOSING
	VWF:RCo		FVIII:C			
	Up to 72 hours post surgery	After 72 hours post surgery	Up to 72 hours post surgery	After 72 hours post surgery		
MINOR	≥30%	–	>40%	–	48 hours	Every 12–24 hours/ every other day
MAJOR	>50%	>30%	>50%	>40%	72 hours	

- In case of major bleeding events or major surgeries requiring repeated, frequent infusions, monitoring of FVIII:C levels is recommended, to decide if rFVIII is required for subsequent infusions to avoid excessive rise of FVIII:C

Undesirable effects

During treatment with VEYVONDI the following adverse reactions may occur:

Hypersensitivity or allergic reactions, thromboembolic events, inhibitor formation against VWF.

Undesirable effects: Very common (≥1/10): Headache. Common (≥1/100 to <1/10): Dizziness, vertigo, dysgeusia, tremor, tachycardia, deep vein thrombosis, hypertension, hot flush, vomiting, nausea, pruritus generalised, chest discomfort, infusion site paraesthesia, electrocardiogram T wave inversion, heart rate increased.¹

Undesirable effects of unknown frequency (cannot be estimated from the available data) include:

Anaphylactic reaction, infusion-related reaction (including tachycardia, flushing, rash, dyspnoea, blurred vision).¹
Refer to section 4.8 of the Summary of Product Characteristics.

Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 of the Summary of Product Characteristics.
Known allergic reaction to mouse or hamster proteins.

VWF= von Willebrand factor, FVIII=factor FVIII, FVIII:C=FVIII activity, rFVIII=recombinant FVIII, VWF:RCo=VWF ristocetin cofactor activity, PK=pharmacokinetic
1. VEYVONDI Summary of Product Characteristics. Available at: <https://www.medicines.org.uk/emc/product/11233/smpc>. Accessed March 2024.

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VEYVONDI® (vonico g alfa) 650 IU and 1300 IU powder and solvent for solution for injection

PRESCRIBING INFORMATION FOR GREAT BRITAIN (ENGLAND, SCOTLAND, WALES)

Refer to the Summary of Product Characteristics (SmPC) before prescribing

Presentation: Each vial contains nominally 650 IU and 1300 IU vonico g alfa powder. After reconstitution with 5 mL or 10 mL, respectively, of solvent provided, VEYVONDI contains approximately 130 IU/mL of vonico g alfa.

Indication: VEYVONDI is indicated in adults (age 18 and older) with von Willebrand disease (VWD), when desmopressin (DDAVP) treatment alone is ineffective or not indicated, for the treatment of haemorrhage and surgical bleeding and prevention of surgical bleeding. VEYVONDI should not be used in the treatment of Haemophilia A.

Dosage and administration: Treatment of VWD should be supervised by a physician experienced in the treatment of haemostatic disorders. 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. Dose based on body weight may require adjustment in underweight or overweight patients (refer to the SmPC for dosing calculations). Generally, 1 IU/kg of VEYVONDI raises the plasma VWF:RCo by 0.02 IU/mL (2%). If the patient's baseline plasma FVIII:C level is <40% or is unknown and in all situations where a rapid correction of haemostasis should be achieved, it is necessary to administer a recombinant factor VIII (rFVIII) product with the first infusion of VEYVONDI, in order to achieve a haemostatic plasma level of FVIII:C. However, if an immediate rise in FVIII:C is not necessary, or if the baseline FVIII:C level is sufficient to ensure haemostasis, the physician may decide to omit the co-administration of rFVIII at the first infusion with VEYVONDI. In case of major bleeding events or major surgeries requiring repeated, frequent infusions, monitoring of FVIII:C levels is recommended, to decide if rFVIII is required for subsequent infusions to avoid excessive rise of FVIII:C. For guidance on the treatment of bleeding episodes (on-demand treatment) and prevention of bleeding / haemorrhage and treatment in case of elective surgery, please refer to the SmPC. VEYVONDI should be administered via the intravenous route up to a maximum rate of 4 mL/min. If any reaction, such as tachycardia, occurs that might be related to the administration of the product, the rate of infusion should be reduced or stopped as required by the clinical condition of the patient. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. Known allergic reaction to mouse or hamster proteins. **Warnings and precautions:** In actively bleeding patients it is recommended to co-administer a FVIII product with VEYVONDI as a first line treatment and depending on the FVIII activity levels. **Traceability:** Name and the batch number of the administered product should be clearly recorded. **Hypersensitivity reactions:** Hypersensitivity reactions (including anaphylaxis) have occurred. Patients should be closely monitored and carefully observed for any symptoms throughout the infusion period. If signs and symptoms occur, patients should immediately discontinue use of VEYVONDI and be provided with appropriate supportive care. VEYVONDI contains traces of mouse immunoglobulin and hamster proteins, and rFVIII. Thrombosis and embolism: There is a risk of occurrence of thrombotic events, particularly in patients with known clinical or laboratory risk factors for thrombosis including

low ADAMTS13 levels. Therefore, patients at risk have to be monitored for early signs of thrombosis, and prophylaxis measures against thromboembolism should be instituted according to current recommendations and standard of care. In patients requiring frequent doses of VEYVONDI in combination with rFVIII, FVIII:C activity should be monitored to avoid sustained excessive FVIII:C plasma levels, which may increase the risk of thrombotic events. Any FVIII that would be administered along with VEYVONDI should be a pure FVIII product. A combination with a FVIII product containing von Willebrand factor (VWF) would pose an additional risk of thrombotic events. **Inhibitors:** Patients with VWD, especially type 3, may develop neutralising antibodies (inhibitors) to VWF. If the expected plasma levels of VWF:RCo is not attained, or if bleeding is not controlled with an appropriate dose, an appropriate assay should be performed to determine if a VWF inhibitor is present. In patients with high levels of anti-VWF neutralising antibodies, von Willebrand factor therapy may not be effective and other therapeutic options should be considered to establish haemostasis. Patients who have high-titre binding antibodies (due to previous treatment with plasma-derived VWF) may require a higher dose to overcome the binding antibody effect and such patients could be managed clinically by administration of higher doses of VEYVONDI based on the PK data for each individual patient. **Excipient-related considerations:** VEYVONDI contains 5.2 mg sodium in each 650 IU vial or 10.4 mg sodium in each 1300 IU vial. To be taken into consideration by patients on a controlled sodium diet. **Interactions:** None known. **Fertility, pregnancy and lactation:** **Pregnancy:** Experience in the treatment of pregnant or breast-feeding women is not available. VEYVONDI should be administered to pregnant women only if clearly indicated, taking into consideration that delivery confers an increased risk of haemorrhagic events in these patients. **Breast-feeding:** It is unknown whether VEYVONDI is excreted in human milk. VEYVONDI should be administered to lactating VWF-deficient women only if clearly indicated. Healthcare professionals should balance the potential risks and only prescribe VEYVONDI if needed. **Fertility:** The effects of VEYVONDI on fertility have not been established. **Undesirable effects:** Very common (>1/10): Headache. **Common (>1/100 to <1/10):** Dizziness, vertigo, dysgeusia, tremor, tachycardia, deep venous thrombosis (*serious*), hypertension, hot flush, vomiting, nausea, pruritus generalised, chest discomfort, infusion site paraesthesia, electrocardiogram T wave inversion and heart rate increased. **Other serious undesirable effects (unknown frequency):** Anaphylactic reaction, infusion-related reaction (including tachycardia, flushing, rash, dyspnoea, blurred vision). **Refer to the SmPC for details on full side effect profile and interactions.** **Legal classification:** POM. **UK basic NHS price:** 92p per IU. **Marketing authorisation numbers:** 650 IU: PLGB 34078/0031; 1300 IU: PLGB 34078/0032. **Business Responsible for Sale and Supply:** Takeda UK Ltd, 1 Kingdom Street, London, W2 6BD, United Kingdom. **PI approval code:** pi-02851. **Date of preparation:** April 2024.

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VEYVONDI® (vonicoq alfa) 650 IU and 1300 IU powder and solvent for solution for injection
PRESCRIBING INFORMATION FOR NORTHERN IRELAND
Refer to the Summary of Product Characteristics (SmPC) before prescribing

Presentation: Each vial contains nominally 650 IU and 1300 IU vonicoq alfa powder. After reconstitution with 5 mL or 10 mL, respectively, of solvent provided, VEYVONDI contains approximately 130 IU/mL of vonicoq alfa.

Indication: VEYVONDI is indicated in adults (age 18 and older) with von Willebrand disease (VWD), when desmopressin (DDAVP) treatment alone is ineffective or not indicated, for the treatment of haemorrhage and surgical bleeding and prevention of surgical bleeding. VEYVONDI should not be used in the treatment of Haemophilia A.

Dosage and administration: Treatment of VWD should be supervised by a physician experienced in the treatment of haemostatic disorders. 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. Dose based on body weight may require adjustment in underweight or overweight patients (refer to the SmPC for dosing calculations). Generally, 1 IU/kg of VEYVONDI raises the plasma VWF:RCo by 0.02 IU/mL (2%). If the patient's baseline plasma FVIII:C level is <40% or is unknown and in all situations where a rapid correction of haemostasis should be achieved, it is necessary to administer a recombinant factor VIII (rFVIII) product with the first infusion of VEYVONDI, in order to achieve a haemostatic plasma level of FVIII:C. However, if an immediate rise in FVIII:C is not necessary, or if the baseline FVIII:C level is sufficient to ensure haemostasis, the physician may decide to omit the co-administration of rFVIII at the first infusion with VEYVONDI. In case of major bleeding events or major surgeries requiring repeated, frequent infusions, monitoring of FVIII:C levels is recommended, to decide if rFVIII is required for subsequent infusions to avoid excessive rise of FVIII:C. For guidance on the treatment of bleeding episodes (on-demand treatment) and prevention of bleeding / haemorrhage and treatment in case of elective surgery, please refer to the SmPC. VEYVONDI should be administered via the intravenous route up to a maximum rate of 4 mL/min. If any reaction, such as tachycardia, occurs that might be related to the administration of the product, the rate of infusion should be reduced or stopped as required by the clinical condition of the patient. **Contraindications:**

Hypersensitivity to the active substance or to any of the excipients. Known allergic reaction to mouse or hamster proteins. **Warnings and precautions:** In actively bleeding patients it is recommended to co-administer a FVIII product with VEYVONDI as a first line treatment and depending on the FVIII activity levels. **Traceability:** Name and the batch number of the administered product should be clearly recorded. **Hypersensitivity reactions:**

Hypersensitivity reactions (including anaphylaxis) have occurred. Patients should be closely monitored and carefully observed for any symptoms throughout the infusion period. If signs and symptoms occur, patients should immediately discontinue use of VEYVONDI and be provided with appropriate supportive care. VEYVONDI contains traces of mouse immunoglobulin and hamster proteins, and rFVIII. Thrombosis and embolism: There is a risk of occurrence of thrombotic events, particularly in patients with known clinical or laboratory risk factors for thrombosis including low ADAMTS13 levels. Therefore, patients at risk have

to be monitored for early signs of thrombosis, and prophylaxis measures against thromboembolism should be instituted according to current recommendations and standard of care. In patients requiring frequent doses of VEYVONDI in combination with rFVIII, FVIII:C activity should be monitored to avoid sustained excessive FVIII:C plasma levels, which may increase the risk of thrombotic events. Any FVIII that would be administered along with VEYVONDI should be a pure FVIII product. A combination with a FVIII product containing von Willebrand factor (VWF) would pose an additional risk of thrombotic events. **Inhibitors:** Patients with VWD, especially type 3, may develop neutralising antibodies (inhibitors) to VWF. If the expected plasma levels of VWF:RCo is not attained, or if bleeding is not controlled with an appropriate dose, an appropriate assay should be performed to determine if a VWF inhibitor is present. In patients with high levels of anti-VWF neutralising antibodies, von Willebrand factor therapy may not be effective and other therapeutic options should be considered to establish haemostasis. Patients who have high-titre binding antibodies (due to previous treatment with plasma-derived VWF) may require a higher dose to overcome the binding antibody effect and such patients could be managed clinically by administration of higher doses of VEYVONDI based on the PK data for each individual patient.

Excipient-related considerations: VEYVONDI contains 5.2 mg sodium in each 650 IU vial or 10.4 mg sodium in each 1300 IU vial. To be taken into consideration by patients on a controlled sodium diet. **Interactions:** None known. **Fertility, pregnancy and lactation:**

Pregnancy: Experience in the treatment of pregnant or breast-feeding women is not available. VEYVONDI should be administered to pregnant women only if clearly indicated, taking into consideration that delivery confers an increased risk of haemorrhagic events in these patients. **Breast-feeding:** It is unknown whether VEYVONDI is excreted in human milk. VEYVONDI should be administered to lactating VWF-deficient women only if clearly indicated. Healthcare professionals should balance the potential risks and only prescribe VEYVONDI if needed. **Fertility:** The effects of VEYVONDI on fertility have not been established. **Undesirable effects:** Very common ($\geq 1/10$): Headache. **Common ($>1/100$ to $<1/10$):** Dizziness, vertigo, dysgeusia, tremor, tachycardia, deep venous thrombosis (*serious*), hypertension, hot flush, vomiting, nausea, pruritus generalised, chest discomfort, infusion site paraesthesia, electrocardiogram T wave inversion and heart rate increased. **Other serious undesirable effects (unknown frequency):** Anaphylactic reaction, infusion-related reaction (including tachycardia, flushing, rash, dyspnoea, blurred vision). **Refer to the SmPC for details on full side effect profile and interactions.** **Legal classification:** POM. **UK basic NHS price:** 92p per IU. **Marketing authorisation numbers:** 650 IU: EU/1/18/1298/001; 1300 IU: EU/1/18/1298/002. **Business Responsible for Sale and Supply:** Takeda UK Ltd, 1 Kingdom Street, London, W2 6BD, United Kingdom.

PI approval code: pi-02850
Date of preparation: April 2024

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