▼This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems.

AUSTRALIAN PRODUCT INFORMATION – VEYVONDI® (vonicog alfa) powder and solvent for injection

1. NAME OF THE MEDICINAL PRODUCT

Vonicog alfa

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

VEYVONDI 650 IU powder for injection with solvent vial
Each vial of powder contains nominally 650 International Units (IU) vonicog alfa. After reconstitution with the 5 mL solvent provided, VEYVONDI contains approximately 130 IU/mL.

VEYVONDI 1300 IU powder for injection with solvent vial
Each vial of powder contains nominally 1300 International Units (IU) vonicog alfa. After reconstitution with the 10 mL solvent provided, VEYVONDI contains approximately 130 IU/mL.

The potency of von Willebrand factor (VWF) is measured in IU using the European Pharmacopeia ristocetin cofactor activity assay (VWF:RCo). The ristocetin cofactor activity of recombinant human VWF was determined against the International Standard (WHO) for VWF concentrate. The specific activity of VEYVONDI is approximately 110 IU VWF:RCo/mg protein.

Vonicog alfa is a purified recombinant human von Willebrand factor (rVWF). It is manufactured by recombinant DNA (rDNA) technology in the Chinese Hamster Ovary (CHO) cell line without the addition of any exogenous human-or animal-derived protein in the cell culture process, purification or final formulation.

The product contains only trace amounts of human recombinant coagulation factor VIII (≤ 0.01 IU FVIII/IU VWF:RCo) as determined using the European Pharmacopoeia chromogenic assay for factor VIII (FVIII). Trace quantities of mouse immunoglobulin (murine IgG, from the immunoaffinity purification), host cell (i.e., CHO) protein, rFurin (used to further process rVWF) are also present in the final product.

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS.

3. PHARMACEUTICAL FORM

Powder and solvent for injection.

VEYVONDI is formulated as a sterile, non-pyrogenic white to off-white lyophilised powder for intravenous injection after reconstitution.

The solvent is a clear and colourless solution.

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

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.

4.2 DOSE AND METHOD OF ADMINISTRATION

VEYVONDI is not bioequivalent to plasma-derived von Willebrand factor, and individual patient dosage must be calculated specifically for VEYVONDI.

Treatment of von Willebrand disease (VWD) should be supervised by a physician experienced in the treatment of haemostatic disorders.

Dosage

Dosage and frequency of administration must be individualised according to clinical judgement and based on the patient´s weight, severity and type of bleeding episodes/surgical intervention, as well as both VWF:RCo and FVIII:C levels, and also based on monitoring of appropriate clinical and laboratory measures. Dose based on bodyweight may require adjustment in underweight or overweight patients.

Generally, 1 IU/kg VEYVONDI raises the plasma VWF:RCo by 0.02 IU/mL (2%).

Haemostasis cannot be ensured until factor VIII coagulant activity (FVIII:C) is at least 0.4 IU/mL (≥ 40% of normal activity). Depending on the patient's baseline FVIII:C levels, a single infusion of rVWF will, in a majority of patients, lead to an increase above 40% in endogenous FVIII:C activity within 6 hours and will result in sustaining this level up to 72 hours post infusion. The dose and duration of the treatment depend on the clinical status of the patient, the severity and type of bleeding, and both VWF:RCo and FVIII:C levels. 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, such as treatment of an acute haemorrhage, severe trauma or emergency surgery, it is necessary to administer a recombinant coagulation 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.

Patients should be monitored for the development of VWF or FVIII neutralising antibodies (inhibitors). If suspected VWF activity (VWF:RCo) plasma levels are not attained, or if bleeding is not controlled with an appropriate dose, an assay should be performed to determine if a VWF or FVIII inhibitor is present. See Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE, Neutralising antibodies (inhibitors).

Treatment of bleeding episodes (On demand treatment)

Start of treatment

The first dose of VEYVONDI should be 40 to 80 IU/kg body weight. Replacement levels of VWF:RCo > 0.6 IU/mL (60%) and FVIII:C > 0.4 IU/mL (40%) should be achieved. Dosing guidelines for treatment of minor and major haemorrhages are provided in Table 1.

VEYVONDI should be administered with rFVIII if the FVIII:C levels are < 40%, or are unknown, to control bleeding. 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 0.2 (IU/mL)/(IU/kg). The complete dose of VEYVONDI should be administered followed by rFVIII within 10 minutes. See Section 4.2 for method of administration and Section 6.2 for incompatibilities in relation to co-administration of VEYVONDI and rFVIII.

Calculating dose

VEYVONDI dose [IU] = dose [IU/kg] x weight [kg]

Subsequent infusions

A subsequent dose of 40 IU to 60 IU/kg of VEYVONDI should be infused every 8 to 24 hours as per the dosing ranges in Table 1, or as long as clinically appropriate. In major bleeding episodes, maintain trough levels of VWF:RCo greater than 50% for as long as deemed necessary.

Based on experience from clinical studies, once VWF has been replaced, endogenous FVIII levels will remain normal or near normal as long as VEYVONDI is continued to be administered.

Table 1
Dosing recommendations for the treatment of minor and major haemorrhages

Haemorrhage	Initial dose[a] (IU VWF:RCo/kg body weight)	Subsequent dose
Minor (e.g. epistaxis, oral bleeding, menorrhagia)	40 to 50 IU/kg	40 to 50 IU/kg every 8 to 24 hours (or as long as deemed clinically necessary)
Major[b] (e.g. severe or refractory epistaxis, menorrhagia, gastrointestinal bleeding, central nervous system trauma, haemarthrosis, or traumatic haemorrhage)	50 to 80 IU/kg	40 to 60 IU/kg every 8 to 24 hours for approximately 2-3 days (or as long as deemed clinically necessary)

[a] If rFVIII is administered, see rFVIII package insert for reconstitution and administration instructions.

[b] 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).

Prevention of bleeding/haemorrhage and treatment in case of elective surgery

Prior to surgery

In patients with inadequate levels of FVIII, a dose of 40-60 IU/kg VEYVONDI should be adminsitered 12-24 hours prior to initiating elective surgery (pre-operative dose), to ensure pre-operative endogenous FVIII levels of at least 0.4 IU/mL for minor and at least 0.8 IU/mL for major surgery.

For prevention of excessive bleeding in case of elective surgery, the FVIII:C levels should be assessed within 3 hours prior to initiation of any surgical procedure.

If the FVIII:C levels are at the recommended target level of:

- at least 0.4IU/mL for minor and oral surgery and
- at least 0.8 IU/mL for major surgery,

a dose of VEYVONDI alone should be administered within 1 hour prior to the procedure.

If the FVIII:C levels are not at the recommended target levels, rFVIII should be administered in addition to VEYVONDI to raise VWF:RCo and FVIII:C, within 1 hour prior to the procedure.

Please refer to Table 2 for FVIII:C recommended target levels. The dose depends on VWF and FVIII levels of the patient, the type and severity of the expected bleeding.

Table 2
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

Type of surgery	VWF:RCo target peak plasma level	FVIII:C target peak plasma level[a]	Calculation of rVWF dose (to be administered within 1 hour prior to surgery) (IU VWF:RCo required)
Minor	0.50 – 0.60 IU/mL	0.40 – 0.50 IU/mL	Δ[b] VWF:RCo x BW(kg)/IR[c]
Major	1 IU/mL	0.80 – 1 IU/mL	Δ[b] VWF:RCo x BW(kg)/IR[c]

[a] Additional rFVIII may be required to attain the recommended FVIII:C target peak plasma levels. Dosing guidance should be done based on the IR.

[b] Δ = Target peak plasma VWF:RCo – baseline plasma VWF:RCo

[c] IR = Incremental Recovery as measured in the subject. If the IR is not available, assume an IR of 0.2 IU/mL per IU/kg.

During and after surgery

After the initiation of the surgical procedure, the VWF:RCo and FVIII:C plasma levels should be monitored and the intra-and post-operative substitution regimen should be individualised according to the PK results, intensity and duration of the haemostatic challenge, and the institution's standard of care. In general, the frequency of VEYVONDI dosing for post-operative substitution should range from twice a day to every 48 hours.

Please refer to Table 3 for treatment recommendations for subsequent maintenance doses.

Table 3
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 during and after surgery

Type of surgery	VWF:RCo target trough plasma level		FVIII:C target trough plasma level		Minimum duration of treatment	Frequency of dosing
	Up to 72 hours post-surgery	After 72 hours post-surgery	Up to 72 hours post-surgery	After 72 hours post-surgery		
Minor	≥ 0.30 IU/mL	–	> 0.40 IU/mL	–	48 hours	Every 12–24 hours to every other day
Major	> 0.50 IU/mL	> 0.30 IU/mL	> 0.50 IU/mL	> 0.40 IU/mL	72 hours	Every 12–24 hours to every other day

Method of administration

VEYVONDI is for intravenous use. The reconstituted product should be inspected visually prior to administration. The reconstituted solution should be clear, colorless solution, free from particles. Do not administer if particulate matter, or discoloration or cloudiness is observed.

The rate of administration should be slow enough to ensure the comfort of the patient, up to a maximum of 4 mL/min.

The patient should be observed for any immediate reaction. 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.

When co-administration of rVWF and rFVIII is considered necessary, they can be pre-mixed in a single syringe to achieve the appropriate dose. The contents of each vial of rVWF and rFVIII can be drawn into a single syringe by using a separate unused reconstitution device (see Section 6.2 INCOMPATIBILITIES).

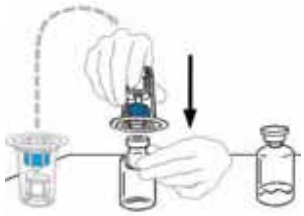
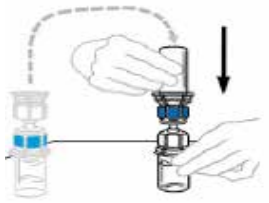
Instructions for use

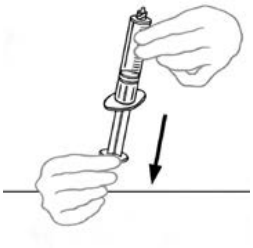
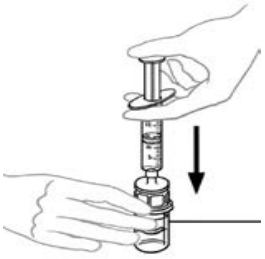
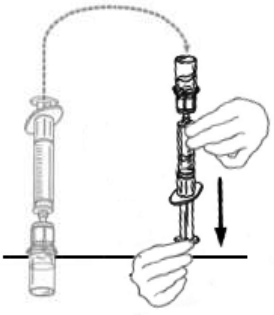
General Instructions

- Check the expiry date. Do not use after the expiry date stated on the labels and carton.
- Ensure that the VEYVONDI powder vial and the solvent vial are at room temperature prior to preparation.
- Use antiseptic technique (clean and low-germ conditions) and a flat work surface during the reconstitution procedure. Wash your hands and put on clean exam gloves (the use of gloves is optional).
- Use the reconstituted product (after mixing the powder with the supplied solvent) as soon as possible and within three hours. The reconstituted product may be stored at room temperature not to exceed 25◦C for up to three hours.
- The reconstituted solution should be inspected visually prior to administration.
- Use plastic syringes with this product because proteins in the product tend to stick to the surface of glass syringes.
- Do not mix VEYVONDI with other medicinal products except for rFVIII (see Section 6.2 INCOMPATIBILITIES).

Reconstitution

1.	Remove the caps from the VEYVONDI powder and solvent vials to expose the center of the rubber stoppers.	
2.	Disinfect each stopper with a separate sterile alcohol swab by wiping the stopper for several seconds. Allow the rubber stopper to dry. Place the vials on a flat surface.	

3.	Open the Mix2Vial device package by completely peeling away the lid, without touching the inside of the package. Do not remove the Mix2Vial device from the package.	
4.	Turn the package with the Mix2Vial device upside down and place it over the top of the solvent vial. Firmly insert the blue plastic spike of the device into the center of the solvent vial stopper by pushing straight down. Grip the package at its edge and lift it off the Mix2Vial device. Be careful not to touch the clear plastic spike. The solvent vial now has the Mix2Vial device connected to it and is ready to be connected to the VEYVONDI powder vial.	
5.	To connect the solvent vial to the VEYVONDI powder vial, turn the solvent vial over and place it on top of the vial containing VEYVONDI powder. Fully insert the clear plastic spike into the VEYVONDI powder vial stopper by firmly pushing straight down. This should be done right away to keep the liquid free of germs. The solvent will flow into the VEYVONDI powder vial by vacuum. Check that all the solvent has transferred. Do not use if the vacuum has been lost and the solvent does not flow into the VEYVONDI powder vial.	
6.	Gently and continuously swirl the connected vials or allow the reconstituted product to stand for 5 minutes then gently swirl to ensure the powder is completely dissolved. Do not shake. Shaking will adversely affect the product. Do not refrigerate after reconstitution.	
7.	Disconnect the two sides of the Mix2Vial from each other by holding the clear plastic side of the Mix2Vial device attached to the VEYVONDI vial with one hand and the blue plastic side of the Mix2Vial device attached to the solvent vial with the other hand. Turn the blue plastic side counter-clockwise and gently pull the two vials apart. Do not touch the end of the plastic connector attached to the VEYVONDI vial containing the dissolved product. Place the VEYVONDI vial on a flat work surface. Discard the empty solvent vial.	

8.	Draw air into the empty, sterile disposable plastic syringe by pulling back on the plunger. The amount of air should equal the amount of reconstituted VEYVONDI that you will withdraw from the vial.	
9.	Place the VEYVONDI vial (containing the reconstituted solution) on your flat work surface, connect the syringe to the clear plastic connector and turning the syringe clockwise.	
10.	Hold the vial with one hand and use the other hand to push all the air from the syringe into the vial.	
11.	Flip connected syringe and VEYVONDI vial so the vial is on top. Be sure to keep the syringe plunger pressed in. Draw the VEYVONDI into the syringe by pulling plunger back slowly.	
12.	Do not push and pull solution back and forth between syringe and vial. Doing so may harm the medicine. When ready to infuse, disconnect the syringe by turning it counter-clockwise. Inspect the syringe visually for particulate matter; the solution should be clear and colourless. If flakes or particles are seen, do not use the solution and notify Shire Customer Service.	

13.	If you need more than one vial of VEYVONDI to make up your dose: - Leave the syringe attached to the vial until an additional vial is prepared. - Use the reconstitution steps above (2 to 8) to prepare the additional vial of VEYVONDI using a fresh Mix2Vial device for each vial.
14.	The contents of two vials may be drawn into a single syringe. NOTE: When pushing air into a second vial of VEYVONDI to be pooled into a syringe, orient the vial and connected syringe with the vial on top.

Administration

Inspect the prepared solution in the syringe for particulate matter and discoloration prior to administration. The solution should be clear, colourless and free from particles. It is not uncommon for a few flakes or particles to remain in the product vial after reconstitution. The filter included in the Mix2Vial device removes those particles completely. Filtration does not influence dosage calculations. The solution in the syringe should not be used if it is cloudy or contains flakes or particles after filtration.

1. Attach the infusion needle to a syringe containing VEYVONDI solution. For comfort, a winged (butterfly) infusion set is preferred. Point the needle up and remove any air bubbles by gently tapping the syringe with your finger and slowly and carefully pushing air out of the syringe and needle.
2. Apply a tourniquet and get the infusion site ready by wiping the skin well with a sterile alcohol swab.
3. Insert the needle into the vein and remove the tourniquet. Slowly infuse VEYVONDI. Do not infuse any faster than 4 mL per minute. Disconnect the empty syringe. If your dose requires multiple syringes, attach and administer each additional syringe of VEYVONDI one at a time.

   NOTE:

   Do not remove butterfly needle until all syringes have been infused and do not touch the Luer port that connects to the syringe.

   If rFVIII has been prescribed, administer rFVIII within 10 minutes after infusion of VEYVONDI has been completed. When co-administration of VEYVONDI and rFVIII is considered necessary, see Section 6.2 for incompatibilities.
4. Take the needle out of the vein and use sterile gauze to put pressure on the infusion site for several minutes.

In case large volumes of VEYVONDI are required, it is possible to pool two vials of VEYVONDI together. The contents of each reconstituted vial can be drawn in a single syringe. However, in these cases the initially reconstituted solution of VEYVONDI should not be diluted any further.

The solution should be slowly administered intravenously not exceeding 4 mL/min.

Do not recap the needle. See section 6.6 SPECIAL PRECAUTIONS FOR DISPOSAL.

4.3 CONTRAINDICATIONS

Hypersensitivity to the active substance or to any of the excipients listed in Section 6.1 LIST OF EXCIPIENTS.

Known allergic reaction to mouse or hamster proteins.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

In actively bleeding patients, it is recommended to co-administer a rFVIII product with VEYVONDI as a first line treatment and depending on the FVIII activity levels (see Section 4.2 DOSE AND METHOD OF ADMINISTRATION).

Traceability

In order to improve the tracebility of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Hypersensitivity reactions

Hypersensitivity reactions (including anaphylaxis) have occurred. Patients and/or their caregivers should be informed of the early signs of hypersensitivity reactions, which may include but are not limited to tachycardia, tightness of the chest, wheezing and/or acute respiratory distress, hypotension, generalised urticaria, pruritus, rhinoconjunctivitis, angioedema, lethargy, nausea, vomiting, paresthesia, restlessness, and may progress to anaphylactic shock. In case of shock, standard medical treatment for shock should be implemented.

Patients should be closely monitored and carefully observed for any symptoms throughout the infusion period. If signs and symptoms of severe allergic reactions occur, immediately discontinue administration of VEYVONDI and provide appropriate supportive care.

Adequate medical treatment and provisions should be available for immediate use for a potential anaphylactic reaction, especially for patients with a history of allergic reactions.

VEYVONDI contains trace amounts of mouse immunoglobulin G (murine IgG) and Hamster proteins (less than or equal to 2 ng/IU VEYVONDI). Patients treated with this product may develop hypersensitivity reactions to these non-human mammalian proteins. VEYVONDI contains trace amounts of 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. See Section 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS), Thrombogenicity.

In patients requiring frequent doses of VEYVONDI in combination with rFVIII, plasma levels for 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 (i.e. rFVIII) product. A combination with a FVIII product containing VWF would pose an additional risk of thrombotic events.

Neutralising antibodies (inhibitors)

Patients with VWD, especially Type 3, may develop neutralising antibodies (inhibitors) to VWF. If the expected plasma levels of (VWF:RCo) are not attained, or if bleeding is not controlled with an appropriate dose, an appropriate assay should be performed to determine if an anti-VWF antibody is present. In patients with high levels of anti-VWF antibodies, VWF therapy may not be effective and other therapeutic options should be considered.

Treatment of VWD patients who have high-titer 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

This medicinal product contains 5.2 mg sodium in each 650 IU vial or 10.4 mg sodium in each 1300 IU vial. This is equivalent to 2.2% of the WHO recommended maximum daily intake of 2 g sodium for an adult, assuming a body weight of 70 kg and a dose of 80 IU/kg body weight. This is to be taken into consideration by patients on a controlled sodium diet.

Use in hepatic impairment

Subjects with significant liver disease were excluded from participation in the clinical trials. No analyses of the intrinsic effects of hepatic impairment on pharmacokinetic outcomes have been conducted.

Use in renal impairment

Subjects with renal disease (with a serum creatinine level ≥ 2 mg/dL) were excluded from participation in the clinical trials. No analyses of the intrinsic effects of renal impairment on pharmacokinetic outcomes have been conducted.

Use in the elderly

There is insufficient data to recommend the use of VEYVONDI in elderly patients (aged 65 and over). Clinical trials of VEYVONDI did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently compared to younger subjects.

Paediatric use

No data available. The safety and efficacy of VEYVONDI in children aged 0 to 18 years have not yet been established.

Effects on laboratory tests

In clinical trials, no clinically significant abnormalities in laboratory parameters were considered to be related to VEYVONDI.

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

No interaction studies have been performed with VEYVONDI. No interactions of human von Willebrand factor products with other medicinal products are known.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

Animal reproduction studies have not been conducted with VEYVONDI.

The effects of VEYVONDI on fertility have not been established.

Use in pregnancy

Australian Pregnancy Categorisation (Category B2)

Experience in the treatment of pregnant women is not available. Animal embryofetal development studies with vonicog alfa have not been performed. Vonicog alfa was shown not to cross the human placenta in an *ex vivo* perfusion model. 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.

Use in lactation

It is unknown whether vonicog alfa is excreted in human milk. Therefore, 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.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

VEYVONDI has no or negligible influence on the ability to drive and use machines.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Summary of the safety profile

During treatment with VEYVONDI, adverse reactions may occur. These include: Hypersensitivity or allergic reactions, thromboembolic events, inhibitor formation against VWF.

Tabulated summary of adverse reactions

The adverse drug reactions (ADR) presented in Table 4 have been identified in 80 patients with von Willebrand disease from a prospective, multicentre, controlled, randomised Phase 1 dose escalation study (070701) evaluating PK, safety and tolerability in severe VWD, a prospective, multicentre, part randomised Phase 3 pivotal study (071001) to assess the PK, safety, and efficacy in the treatment of bleeding episodes in severe VWD, and a Phase 3 surgical study (071101).

Frequency categories are defined according to the following convention: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000), very rare (< 1/10,000), not known (cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in the order of decreasing seriousness.

Table 4
Summary of adverse reactions reported in clinical trials with VEYVONDI in VWD

MedDRA System Organ Class (SOC)	Adverse reaction by Preferred Term (PT)	Frequency category by subject	Number and frequency by subject[a] (N=80[c]) n (%)	Number and frequency by infusion[b] (N=476) n (%)
Nervous system disorders	Dizziness	Common	3 (3.75)	3 (0.63)
	Vertigo	Common	2 (2.50)	3 (0.63)
	Dysgeusia	Common	1 (1.25)	1 (0.21)
	Tremor	Common	1 (1.25)	1 (0.21)
Cardiac disorders	Tachycardia	Common	1 (1.25)	1 (0.21)
Vascular disorders	Deep venous thrombosis	Common	1 (1.25)	2 (0.42)
	Hypertension	Common	1(1.25)	2 (0.42)
	Hot flush	Common	1 (1.25)	1 (0.21)
Gastrointestinal disorders	Vomiting	Common	3 (3.75)	4 (0.84)
	Nausea	Common	3 (3.75)	3 (0.63)
Skin and subcutaneous tissue disorders	Pruritus generalised	Common	2 (2.50)	2 (0.42)
General disorders and administration site conditions	Chest discomfort	Common	1 (1.25)	1 (0.21)
	Infusion site paraesthesia	Common	1 (1.25)	1 (0.21)
Investigations	Electrocardiogram T wave inversion	Common	1 (1.25)	1 (0.21)
	Heart rate increased	Common	1 (1.25)	1 (0.21)

[a] **Frequency by Subject:** Total number of subjects experiencing the AE (related and unrelated) divided by total number of subjects (N) and multiplied by 100.

[b] **Frequency by Infusion:** Total number of unique infusions after which at least one AE was reported of the

MedDRA System Organ Class (SOC)	Adverse reaction by Preferred Term (PT)	Frequency category by subject	Number and frequency by subject[a] (N=80[c]) n (%)	Number and frequency by infusion[b] (N=476) n (%)

respective ADR preferred term divided by total number of infusions (N) and multiplied by 100.

[c] **Total number of subjects analysed:** 31 subjects in study 070701, 37 subjects in study 071001 and 15 subjects in study 071101 were treated with VEYVONDI. Among these, 3 subjects participated in more than one study.

Description of selected adverse reactions

Hypersensitivity

There is a possibility of developing hypersensitivity or allergic reactions (which may include angioedema, burning and stinging at the infusion site, chills, flushing, rhinoconjunctivitis, generalised urticaria, headache, hives, hypotension, lethargy, nausea, restlessness, tachycardia, tightness of the chest, tingling, vomiting, wheezing) which may in some cases progress to anaphylaxis (including shock).

Patients with VWD, especially Type 3, may very rarely develop neutralising antibodies (inhibitors) to VWF. If such inhibitors occur, the condition may manifest itself as an inadequate clinical response. Such antibodies may occur in close association with hypersensitivity or anaphylactic reactions. Therefore, patients experiencing hypersensitivity or anaphylactic reactions should be tested and evaluated for the presence of an inhibitor.

In all such cases, it is recommended that a specialised haemophilia centre be contacted.

Thrombogenicity

In clinical trials, one case of clinically asymptomatic deep vein thrombosis (DVT) was reported for a subject in the surgery study who had total hip replacement. In addition, one post-marketing case of DVT has been reported spontaneously in an elderly patient.

Immunogenicity

The immunogenicity of VEYVONDI was assessed in clinical trials by monitoring the development of neutralising antibodies against VWF and FVIII, as well as binding antibodies against VWF, Furin, Chinese Hamster Ovary (CHO) protein and mouse IgG. No treatment-emergent development of neutralising antibodies against human VWF or neutralising antibodies against human rFVIII was observed. One of the 80 subjects who received VEYVONDI perioperatively in clinical studies developed treatment-emergent binding antibodies against VWF following a surgery for whom no adverse events or lack of haemostatic efficacy has been reported. Binding antibodies against impurities such as rFurin, CHO-protein or mouse IgG were not observed after treatment with VEYVONDI.

The long-term safety profile of VEYVONDI has not been established yet.

Post-marketing experience

Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

The following are the most common post-marketing ADRs reported in association with VEYVONDI treatment with an unknown frequency, listed by MedDRA System Organ Class (SOC), then by Preferred Term.

IMMUNE SYSTEM DISORDERS:
Anaphylactic reaction

GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS:
Infusion-related reaction (IRR), clinically manifested by the following symptoms: tachycardia, flushing, rash, dyspnea, and blurred vision.

In the 2 spontaneous post-marketing cases reported of infusion related reactions, the symptoms resolved and the patients fully recovered in approximately 20 minutes to 4 hours upon stopping the infusion.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

No symptoms of overdose with VWF have been reported. Thromboembolic events may occur in case of major overdose.

For information on the management of overdose, contact the Poisons Information Centre on 131126 (Australia).

5. PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Antihaemorrhagics: blood coagulation factor von Willebrand factor.

ATC code: B02BD10

Mechanism of action

von Willebrand factor is the carrier molecule for factor VIII, an essential cofactor of secondary haemostasis that leads to the fibrin clot formation, and facilitates platelet adhesion to sub-endothelium at sites of vascular injury.

Vonicog alfa is a recombinant human von Willebrand factor (rVWF). Vonicog alfa behaves in the same way as endogenous VWF.

Administration of vonicog alfa allows correction of the haemostatic abnormalities exhibited by patients who suffer from VWF deficiency (VWD) at two levels:

- Vonicog alfa re-establishes platelet adhesion to the vascular sub-endothelium at the site of vascular damage (as it binds both to the vascular sub-endothelium matrix (e.g. collagen) and to the platelet membrane), providing primary haemostasis as shown by the shortening of the bleeding time. This effect occurs immediately and is known to depend to a large extent on the level of polymerisation of the protein.

- Vonicog alfa produces delayed correction of the associated FVIII deficiency. Administered intravenously, vonicog alfa binds to endogenous FVIII (which is produced normally by the patient), and by stabilising this factor, avoids its rapid degradation. Because of this, administration of vonicog alfa restores the FVIII:C level to normal as a secondary effect. After the first infusion, the FVIII:C rises above 40% within 6 hours and peaks within 24 hours in a majority of patients, depending on the baseline FVIII:C level.

The adhesive activity of rVWF depends on the size of its multimers, with ultra-large multimers being the most effective in supporting interactions with collagen and platelet receptors.

Clinical trials

The clinical safety, efficacy and PK data were assessed in 3 completed trials, (070701, 071001 and 071101) which enrolled patients with VWD. A total of 92 unique subjects (80 unique subjects with VWD in studies 070701, 071001 and 071101 and 12 subjects with Haemophilia A in study 071104) were exposed to VEYVONDI during clinical development.

Study 071001 (Phase 3 VWD)

A Phase 3, multicentre part-randomised clinical study to assess the PK, safety and efficacy of rVWF:rFVIII and rVWF in the treatment of bleeding episodes in adult subjects with severe Type 3 and severe non-Type 3 VWD. The study consisted of 2 parts; Part A consisted of PK assessment alone (Arm 2: PK50 only [without treatment of bleeding episodes]), or PK assessments (Arm 1: PK50 and Arm 3: PK80) plus on-demand treatment period(s) of 6 months for bleeding episodes, or Arm 4: on demand treatment for bleeding episodes only. Patients receiving treatment for PK assessments and/or bleeding episodes in Part A were to be entered into Part B to continue on-demand treatment for bleeding episodes for 6 additional months for a total of 12 months in the study.

A total of 193 bleeding episodes were reported in 22/37 subjects exposed to VEYVONDI and the haemostatic efficacy data are available on 192 bleeding episodes (1 bleeding episode in 1

subject was excluded because the subject received a plasma-derived VWF product for the third infusion; therefore, the analysis was conducted on 192 bleeding episodes).

The primary efficacy endpoint was the number of subjects with treatment success for control of bleeding episodes. Treatment success was defined as a mean efficacy rating score of less than 2.5 for all bleeding episodes in a subject treated with VEYVONDI (with or without ADVATE [octocog alfa, a rFVIII]) during the trial period. The efficacy rating was assessed using a pre-specified 4 point rating scale comparing the prospectively estimated number of infusions needed to treat the bleeding episodes as assessed by the investigator to the actual number of infusions administered.

Secondary efficacy measures were the number of treated bleeding episodes with an efficacy rating of 'excellent' or 'good', the number of infusions and number of units of VEYVONDI, administered with or without ADVATE, per bleeding episode.

The primary efficacy assessments of treatment success for bleeds were made prospectively and excluded gastrointestinal (GI) bleeds. Eighteen subjects were included in the primary outcome assessment after excluding 2 subjects with only GI bleed (and no other bleeds requring VEYVONDI), and 2 subjects in whom th enumber of infusions to control a bleed was estimated retrospectively. The rate of subjects (n=18) with treatment success was 100% (95% CI 81.5 to 100).

Sensitivity analyses of treatment success for bleeding episodes including GI bleeds and those bleeding episodes for which the investigator made retrospective assessment of the number of infusions required (n=22: 17 with type 3 VWD, 4 with type 2A VWD and 1 with type 2N VWD) confirmed the primary analysis, with a 100% treatment success rate for each scenario.

All bleeding episodes treated with VEYVONDI and ADVATE or VEYVONDI alone were controlled with an efficacy rating of excellent (96.9%) or good (3.1%). Control of bleeding episodes was consistent across all degrees of bleeding severity.

For an overview of haemostatic efficacy by bleeding severity and number of infusions required to treat a bleeding episode refer to Table 5.

Table 5
Number of infusions by severity of bleeding episodes[a]

Number of infusions per bleed	Severity of bleeding episodes				
	Minor n (%) n=122	**Moderate n (%) n=61**	**Major/Severe n (%) n=7**	**Unknown n (%) n=2**	**All n (%) n=192**
1	113 (92.6%)	41 (67.2%)	1 (14.3%)	2 (100%)	157 (81.8%)
2	8 (6.6%)	13 (21.3%)	4 (57.1%)	0 (0.0)	25 (13.0%)
3	1 (0.8%)	6 (9.8%)	2 (28.6%)	0 (0.0)	9 (4.7%)
4	0 (0.0)	1 (1.6%)	0 (0.0)	0 (0.0)	1 (0.5%)
Median	1	1	2	1	1
Range	1-3	1-4	1-3	1-1	1-4

[a] One subject received plasma-derived VWF for one bleeding episode for the 3rd infusion and therefore it was excluded from the total number (193) of bleeding episodes in Table 5.

The median cumulative dose of VEYVONDI with or without ADVATE administered per bleeding episodes (n=174) was 48.2 IU/kg (90% CI, 43.9 to 50.2 IU/kg). The median actual dose of VEYVONDI with ADVATE administered per bleeding episode (n=166) was 46.5 (90% CI, 43.3 to 48.2) IU/kg and 33.6 (90% CI, 32.4 to 36.8) IU/kg respectively. The median actual dose of VEYVONDI alone administered per bleeding episode (n=30) was 52.8 (90% CI, 52.6 to 55.7) IU/kg.

In relation to bleeding severity, the median cumulative dose of VEYVONDI to treat a bleeding episode was 43.3 (range, 25.2 to 158.2) IU/kg for minor bleeding episodes (n=122), 52.7 (range, 23.8 to 184.9) IU/kg for moderate bleeding episodes (n=61), 100.0 (range, 57.5 to 135.0) IU/kg for major bleeding episodes (n=7).

Table 6 summarises the data obtained for number of infusions and efficacy rating per bleeding episode by location.

Table 6
Efficacy by bleeding episode location

Bleeding episode by location (n)	Median number of infusions (range)	Rating (%)
Joint (n=59)	1 (1 to 3)	Excellent (96.6%) Good (3.4%)
GI (n=6)	1 (1 to 2)	Excellent (83.3%) Good (16.7%)
Mucosal: Genital tract female (n=45)	1 (1 to 4)	Excellent (97.8%) Good (2.2%)
Mucosal: Nasopharyngeal (n=42)	1 (1 to 2)	Excellent (97.6%) Good (2.4%)
Mucosal: Mouth and oral cavity (n=26)	1 (1 to 43)	Excellent (100.0%) Good (0%)

Study 071101 (Phase 3 VWD – Surgery)

Haemostatic efficacy of VEYVONDI was assessed in a Phase 3 prospective, open-label multicentre study to evaluate efficacy and safety of VEYVONDI with or without ADVATE in elective surgical procedures in adults (age 18 years and older) diagnosed with severe VWD. A total of 24 subjects were enrolled (signed informed consent) and screened, 15 subjects were treated with VEYVONDI, and 15 subjects completed the study. A minimum of 15 subjects with severe VWD were enrolled, of whom at least 10 underwent major surgical procedures.

All subjects received a dose of 40 to 60 IU/kg rVWF:RCo 12 to 24 hours before surgery. Within 3 hours prior to surgery, the subject's FVIII:C levels were assessed with a target of 0.30 IU/mL for minor and oral surgeries and 0.60 IU/mL for major surgeries. Within 1 hour prior to surgery, subjects received a dose of VEYVONDI with or without ADVATE (depending on the target FVIII:C levels at the 3 hour assessment). VWF and FVIII incremendal recovery and $T_{1/2}$ for each subject, when known, were used to guide the initial dose and subsequent doses.

The primary outcome measure was the overall assessment of haemostatic efficacy assessed by the investigator (haemophilia physician) 24 hours after last perioperative VEYVONDI infusion or at completion of day 14 visit, whichever occurred earlier, was summarised by the percentage

of subjects in each efficacy category ("excellent", "good", "moderate" and "none"). Point estimate and corresponding 90% two-sided exact confidence interval (CI) was calculated for the rate of subjects with an overall assessment of haemostatic efficacy. All 15 subjects treated with VEYVONDI (with or without ADVATE) for major (10), minor (4), and oral (1) elective surgical procedures had overall haemostatic efficacy ratings of "excellent" or "good". Most (73.3%) subjects had "excellent" overall haemostatic efficacy ratings; of these, 7 underwent major surgery and 4 underwent minor surgery. The remaining 26.7% subjects had "good" overall haemostatic efficacy ratings: 3 underwent major surgery and 1 underwent oral surgery. All 8 subjects with VWD Type 3, the subtype classified as absolute VWF deficiency, had overall haemostatic effiacy ratings of "excellent" (87.5%) or "good" (12.5%).

Intraoperative haemostatic efficacy ratings were also rated as "excellent" or "good" for all 15 treated subjects. Most (86.7%) subjects had "excellent" intraoperative haemostatic efficacy ratings; of these, 8 underwent major surgery, 4 underwent minor surgery, and 1 underwent oral surgery. Two (13.3%) subjects who underwent major surgery had "good" intraoperative haemostatic efficacy ratings. Intraoperative haemostatic efficacy was rated as "excellent" or "good" for all subjects with VWD Type 3: "excellent" for 7 (87.5%) subjects and "good" for 1 (12.5%) subject. Only 1 subject received an intraoperative dose of VEYVONDI (18.1 IU/kg) and ADVATE (8.1 IU/kg).

For patients treated with VEYVONDI (with or without ADVATE), the median total postoperative dose within the first 7 days after surgery was 114.2 IU/kg with a range of 23.8 to 318.9 IU/kg (n=13) and 76.2 IU/kg with a range of 23.8 to 214.4 IU/kg for the next 7 postoperative days (n=8).

For patients treated with VEYVONDI alone, the median total postoperative dose within the first 7 days after surgery was 103.4 IU/kg with a range of 23.8 to 318.9 IU/kg (n=12) and 94.5 IU/kg with a range of 23.8 to 214.4 IU/kg for the next 7 postoperative days (n=7).

Table 7 summarises the data obtained for VEYVONDI treatment by surgery type.

Table 7
VEYVONDI treatment summary by surgery type[a]
(Study 071101: Safety Analysis Set)

Parameter	Minor		Major		Oral		Overall	
	Mean	Median (Min-Max)	Mean	Median (Min-Max)	Mean	Median (Min-Max)	Mean	Median (Min-Max)
Number of doses to treat surgery	3.0	3.0 (2-4)	9.3	9.0 (4-15)	5.0	5.0 (5-5)	7.3	6.0 (2-15)
Exposure Days to treat surgery	3.0	3.0 (2-4)	8.6	8.0 (4-15)	4.0	4.0 (4-4)	6.8	6.0 (2-15)
Pre-operative dose 12-24 h before surgery [IU/kg]	57.3	57.2 (55.0-59.9)	49.8	49.3 (37.4-57.6)	36.1	36.1 (36.1-36.1)	50.9	55.0 (36.1-59.9)
Pre-operative dose 1 h before surgery [IU/kg]	33.2	39.3 (8.0-46.4)	42.8	37.6 (15.7-82.7)	18.1	18.1 (18.1-18.1)	38.6	35.8 (8.0-82.7)
Intra-operative dose [IU/kg]	NA	NA	NA	NA	18.1	18.1 (18.1-18.1)	18.1	18.1 (18.1-18.1)

Parameter	Minor		Major		Oral		Overall	
	Mean	Median (Min-Max)	Mean	Median (Min-Max)	Mean	Median (Min-Max)	Mean	Median (Min-Max)
Total Post-operative dose (Days 0-14) [IU/kg]	79.3	79.3 (42.8-115.9)	225.7	233.9 (47.7-533.3)	36.1	36.1 (36.1-36.1)	188.6	197.9 (36.1-533.3)

[a] Infusions to treat surgery refers to the total of the 12-24 hour pre-operative infusions, 1 hour pre-operative initial doses, intra-operative doses and post-operative doses.
Infusions to treat the bleed / maintain haemostasis are taken into account as postoperative infusions.

In this study, 1 subject with VWD Type 3 tested positive for binding antibodies to VWF on post-operative day 7 through study completion, subsequent to receiving an intraoperative transfusion of packed red blood cells during total knee replacement surgery. No subjects developed neutralising antibodies to rFVIII or binding antibodies to CHO, rFurin, or murine IgG.

5.2 PHARMACOKINETIC PROPERTIES

The pharmacokinetics (PK) of VEYVONDI were determined in three clinical studies by assessing the plasma levels of VWF:RCo, von Willebrand Factor Antigen (VWF:Ag), and von Willebrand Collagen Binding Activity (VWF:CB). In all three studies, subjects were evaluated in the non-bleeding state. Sustained increase of FVIII:C was observed by six hours after a single infusion of VEYVONDI.

Table 8 summarises the PK of VEYVONDI after 50 IU/kg VWR:RCo (PK_{50}) or 80 IU/kg VWF:RCo (PK_{80}) infusions . The mean duration of infusion was 16.5 minutes (SD ± 3.51 minutes) for 50 IU/kg (PK_{50}) and 11.8 minutes (± 2.86 minutes) for 80 IU/kg VWF:RCo (PK_{80}).

Table 8
Pharmacokinetic assessment of VWF:RCo[f]

Parameter	Phase 1 PK_{50} VEYVONDI with ADVATE[g] (Study 070701) Mean (95% CI) SD	Phase 3 PK_{50} VEYVONDI (Study 071001) Mean (95% CI) SD	Phase 3 PK_{80} VEYVONDI (Study 071001) Mean (95% CI) SD	Surgery PK_{50} VEYVONDI (Study 071101) Mean (95% CI) SD
$T_{1/2}$[a]	19.3 (14.3; 24.3) 10.99	22.6 (19.5; 25.7) 5.34	19.1 (16.7; 21.5) 4.32	17.8 (12.9; 22.8) 7.34
CL[b]	0.04 (0.03; 0.05) 0.028	0.02 (0.02; 0.03) 0.005	0.03 (0.02; 0.03) 0.009	0.03 (0.02; 0.04) 0.011
IR at C_{max}[c]	1.7 (1.4; 2.0) 0.62	1.9 (1.6; 2.1) 0.41	2.0 (1.7; 2.2) 0.39	2.0 (1.7; 2.3) 0.45
$AUC_{0\text{-}inf}$[d]	1541.4 (1295.7; 1787.2) 554.31	2105.4 (1858.6; 2352.3) 427.51	2939.0 (2533.2; 3344.8) 732.72	1834.4 (1259.0; 2409.7) 856.45
$AUC_{0\text{-}inf}$/Dose[e]	33.4 (27.2; 39.5) 13.87	42.1 (37.3; 46.9) 8.31	36.8 (31.8; 41.8) 8.97	37.5 (25.3; 49.7) 18.14

[a] [hours], [b] [dL/kg/hours], [c] [(U/dL)/(U VWF:RCo/kg)], [d] [(h*U/dL)], [e] [(h*U/dL)/(U VWF:RCo/kg)]

[f] VWF:RCo assays with different sensitivity and working ranges were used:
Phase 1: automated assay 0.08 – 1.50 IU/mL and sensitive manual assay 0.01 – 0.08 IU/mL;
Phase 3: automated assay 0.08 – 1.50 IU/mL

[g] This trial was done using ADVATE, a rFVIII

An exploratory analysis of combined data from studies 070701 and 071001 indicated a statistically significant (at the 5% level) longer mean residence time, a statistically significant (at the 5% level) longer terminal half-life and larger $AUC_{0\text{-inf}}$ regarding VWF:RCo following administration with VEYVONDI (50 IU/kg VWF:RCo) and combined administration of VEYVONDI and ADVATE (50 IU/kg VWF:RCo and 38.5 IU/kg rFVIII) than after administration of pdVWF and pdFVIII (50 IU/kg pdVWF:RCo and 38.5 IU/kg pdFVIII).

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

Vonicog alfa was not mutagenic in bacterial reverse mutation assays, and was not clastogenic *in vitro* in human lymphocytes or *in vivo* in the mouse bone marrow micronucleus test. As a large protein molecule, vonicog alfa is not expected to interact with DNA or other chromosomal material.

Carcinogenicity

Carcinogenicity studies have not been conducted with vonicog alfa. Given the nature of the product, there is no particular concern for carcinogenicity in patients treated with vonicog alfa.

6. PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Powder
Sodium citrate dihydrate
Glycine
Trehalose dihydrate
Mannitol
Polysorbate 80

Solvent
Water for injections

6.2 INCOMPATIBILITIES

Clinical and compatibility studies were conducted to administer VEYVONDI (rVWF) with ADVATE (rFVIII) in the same syringe. The rVWF and rFVIII can be pre-mixed in a single syringe to achieve the appropriate dose, see Section 4.2 DOSE AND METHOD OF ADMINISTRATION, Method of administration).

VEYVONDI must not be mixed with other medicinal products except for rFVIII.

6.3 SHELF LIFE

Unopened vial

In Australia, information on the shelf-life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

After reconstitution

Chemical and physical in-use stability has been demonstrated for 3 hours at 25°C.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Unopened vials

Store below 30°C.
Do not freeze.
Store in the original package in order to protect from light.

After reconstitution

For storage conditions after reconstitution, see Section 6.3 SHELF LIFE – After reconstitution.

6.5 NATURE AND CONTENTS OF CONTAINER

Each pack of VEYVONDI 650 IU contains:

- one powder vial of 650 IU vonicog alfa,
- one solvent vial of 5 mL water for injections and
- one reconstitution device (Mix2Vial)

Each pack of VEYVONDI 1300 IU contains:

- one powder vial of 1300 IU vonicog alfa,
- one solvent vial of 10 mL water for injections and
- one reconstitution device (Mix2Vial)

The powder is supplied in Type 1 glass vial with a butyl rubber stopper. The solvent is supplied in Type 1 glass vial with a chlorobutyl rubber stopper (5 mL solvent) or a bromobutyl rubber stopper (10 mL solvent).

Components used in the packaging of VEYVONDI are not made with natural rubber latex.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

For single use only and for one patient only. Discard unused portion of the product.

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure

VWF is a large multimeric glycoprotein that is normally found in plasma, alpha-granules of platelets and intracellular organelles known as the Weibel Palade bodies. The multimers of VWF range in molecular weight (MW) from 500 to > 20,000 kDa.

VEYVONDI contains VWF expressed from CHO cells. After reduction of disulfide bonds in electrophoretic analysis VEYVONDI appears as a single predominant band having an apparent MW of approximately 260 kDa. In low resolution agarose gel electrophoresis VEYVONDI shows a characteristic ladder of bands also known as multimers.

VEYVONDI is rVWF that contains ultra-large multimers in addition to all of the multimers found in plasma as it is not exposed to proteolysis by ADAMTS13 during the manufacturing process.

CAS number

109319-16-6

7. MEDICINE SCHEDULE (POISONS STANDARD)

Unscheduled (Exempted)

8. SPONSOR

Shire Australia Pty Limited
Shire is now part of Takeda
Level 39
225 George Street
Sydney NSW 2000
Australia

Telephone: 1800 012 612

www.shireaustralia.com.au

9. DATE OF FIRST APPROVAL

20 April 2020

10. DATE OF REVISION

Not applicable.

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
Not applicable.	

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