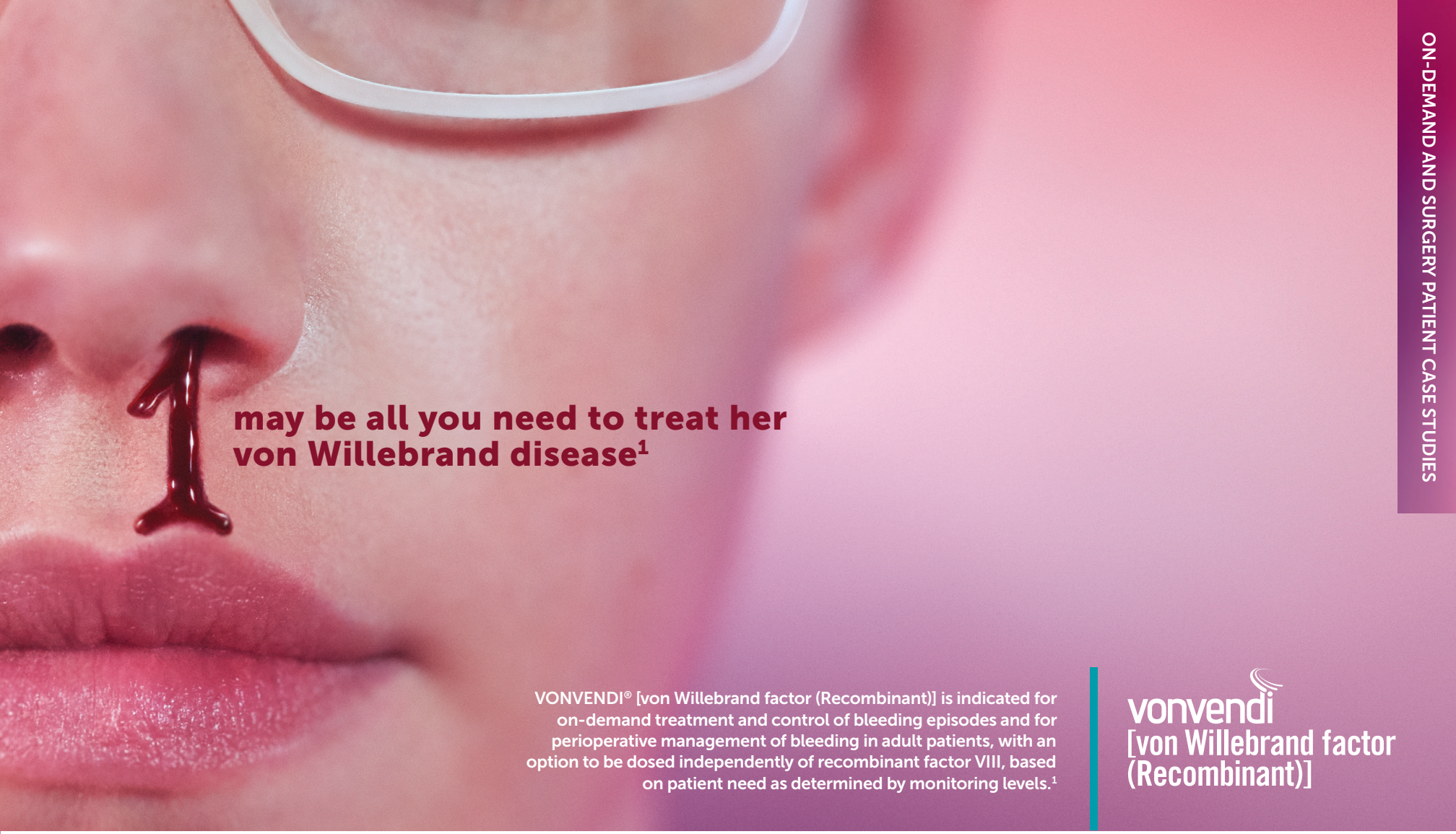


1 may be all you need to treat her von Willebrand disease[1]

VONVENDI® [von Willebrand factor (Recombinant)] is indicated for on-demand treatment and control of bleeding episodes and for perioperative management of bleeding in adult patients, with an option to be dosed independently of recombinant factor VIII, based on patient need as determined by monitoring levels.[1]

vonvendi
[von Willebrand factor (Recombinant)]

Indications

VONVENDI [von Willebrand factor (recombinant)] is a recombinant von Willebrand factor (rVWF) indicated for use in adults (age 18 and older) diagnosed with von Willebrand disease (VWD) for:

- On-demand treatment and control of bleeding episodes
- Perioperative management of bleeding

Selected Important Risk Information

CONTRAINDICATIONS

Do not use in patients who have had life-threatening hypersensitivity reactions to VONVENDI or its components (tri-sodium citrate-dihydrate, glycine, mannitol, trehalose-dihydrate, polysorbate 80, and hamster or mouse proteins).

Please see VONVENDI full Detailed Important Risk Information on page 9.
Please click here for VONVENDI full Prescribing Information.

1 factor may allow for independent dosing[1,a]

Why replace only what is deficient or defective in von Willebrand disease (VWD)—von Willebrand factor (VWF)?

Frequent, repeated administration of VWF/factor VIII (FVIII) complexes in patients with VWD can lead to an excessive rise in FVIII levels; such levels (>200%) have been associated with thromboembolic events in patients who have additional risk factors.[1-4,b]

VONVENDI® [von Willebrand factor (Recombinant)] enables healthcare providers to manage VWF and FVIII levels separately and specifically, based on patient need.[1]

ON DEMAND

For treatment and control of bleeds[1]

VONVENDI may be administered alone if a patient's baseline plasma FVIII:C level is known and is

≥40% or **an immediate rise in FVIII levels is not necessary**

SURGERY

For management of perioperative bleeding[1]

VONVENDI may be administered alone if a patient's presurgical plasma FVIII:C level is

≥30 IU/dL for minor surgery or **≥60 IU/dL for major surgery**

[a]VONVENDI contains only trace amounts of recombinant FVIII (rFVIII).[1]
[b]Additional risk factors include old age, previous thrombosis, obesity, immobility, cancer, orthopedic surgery, estrogen therapy, and the use of antifibrinolytics.[5]

Selected Important Risk Information
WARNINGS AND PRECAUTIONS
Embolism and Thrombosis
Thromboembolic reactions, including disseminated intravascular coagulation, venous thrombosis, pulmonary embolism, myocardial infarction, and stroke, can occur, particularly in patients with known risk factors for thrombosis, including low ADAMTS13 levels. Monitor for early signs and symptoms of thrombosis such as pain, swelling, discoloration, dyspnea, cough, hemoptysis, and syncope, and institute prophylaxis measures against thromboembolism based on current recommendations.

WARNINGS AND PRECAUTIONS (CONTINUED)
Embolism and Thrombosis
In patients requiring frequent doses of VONVENDI in combination with recombinant factor VIII, monitor plasma levels for FVIII:C activity because sustained excessive factor VIII plasma levels can increase the risk of thromboembolic events.

One out of 80 subjects treated with VONVENDI in clinical trials developed proximal deep vein thrombosis in perioperative period after total hip replacement surgery.

Please see VONVENDI full Detailed Important Risk Information on page 9.
Please click here for VONVENDI full Prescribing Information.

1 infusion resolved the majority of bleeds, regardless of bleed location or severity[1]

A Phase 3 prospective, multicenter, open-label study assessed the efficacy and safety of on-demand use of VONVENDI, with and without rFVIII, in adult patients with severe VWD.[1]

100% of patients experienced treatment success (primary endpoint), defined as a mean efficacy rating score of less than 2.5 for all bleeding episodes (18/18; 95% CI, 81.5-100), assessed on a 4-point rating scale (Excellent=1, Good=2, Moderate=3, None=4).[1]

Participants with gastrointestinal bleeds (n=2) and those in whom the number of infusions to control a bleeding episode was estimated retrospectively (n=2) were excluded from the primary analysis.[1]

81.8% (157/192) of bleeds treated were resolved with 1 infusion (median 1, range 1-4).[1]

- Major/severe bleeds were resolved with a median of 2 infusions (range 1-3)[1]

The study protocol stipulated that the first dose of VONVENDI [von Willebrand factor (Recombinant)] be administered together with rFVIII; VONVENDI may be administered alone if an immediate rise in FVIII:C is not necessary, or if the baseline FVIII:C level is ≥40%.[1]

NUMBER OF INFUSIONS BY SEVERITY OF BLEEDING EPISODE[1,a]

Number of infusions per bleed	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] For one bleeding episode, a participant received plasma-derived von Willebrand factor and that episode was therefore not included in the analysis.

vonvendi
[von Willebrand factor (Recombinant)]

Katie: On-demand bleed*

18-year-old female
VWD type 2A
130 lb

"I used to be so outgoing. But lately, I'm either thinking about my VWD or dealing with my VWD. Especially now that I'm going to college, I feel my disease is becoming a cage."
—*Katie*

Intensifying menorrhagia for the past 2 months

History of spontaneous gastrointestinal bleeds

Medical history:
Katie was put on oral contraceptives for consistent heavy menstrual bleeding at the age of 14.[6] As a child she had experienced spontaneous gastrointestinal bleeds, yet von Willebrand disease (VWD) was not suspected until her brother was diagnosed with type 2A; she was formally diagnosed at a hemophilia treatment center (HTC) at 16.[7]

Katie has recently been taken off oral contraceptives because of persistent headaches.[6] A non-hormonal agent is currently being used to control minor bleeds, but major bleeds have historically been difficult to manage and required multiple doses of von Willebrand factor (VWF)/factor VIII (FVIII) complexes.[7,8]

She now presents at an HTC at age 18 with menorrhagia that has already lasted 10 days.[9,10] Katie appears stressed and says her unresolved bleeding is disrupting her daily life.[6] Despite the history of heavy menstrual bleeds, her serum iron levels have been historically normal. These have recently begun to decrease with the intensifying menorrhagia and are now just below normal levels.[6]

*Photo and profile based on a hypothetical patient with VWD.

WARNINGS AND PRECAUTIONS (CONTINUED)

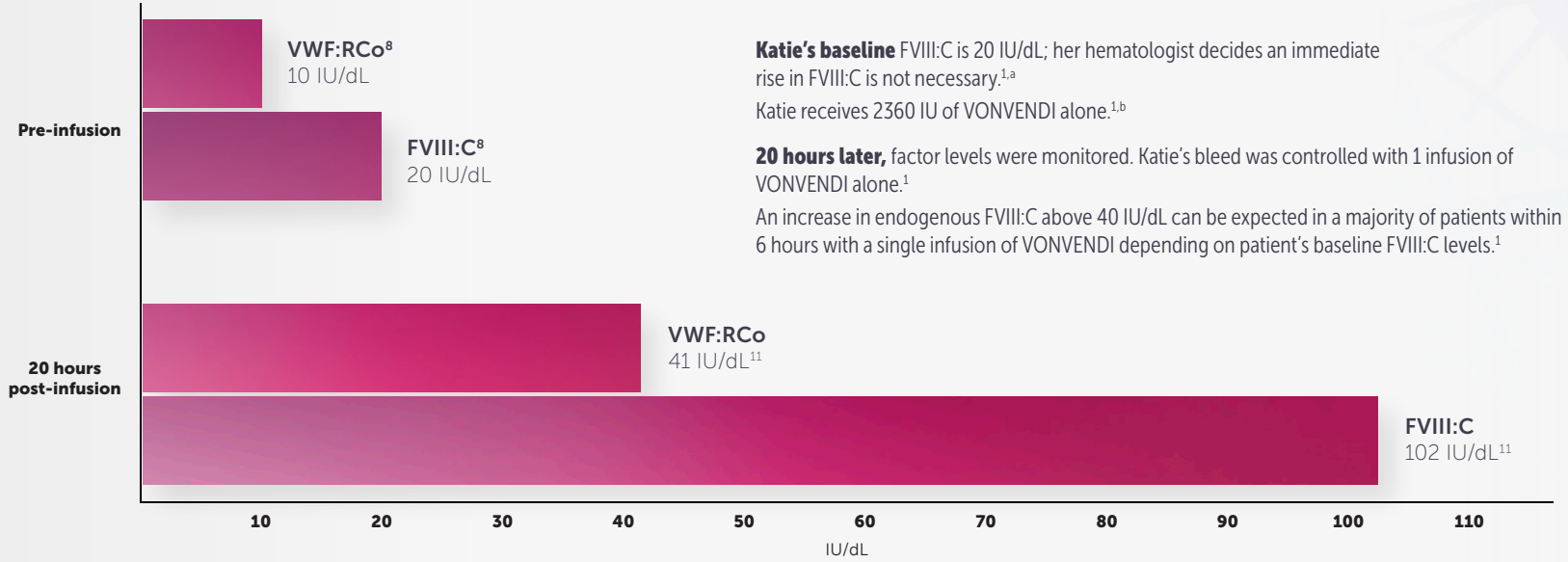
Hypersensitivity Reactions

Hypersensitivity reactions have occurred with VONVENDI. These reactions can include anaphylactic shock, generalized urticaria, angioedema, chest tightness, hypotension, shock, lethargy, nausea, vomiting, paresthesia, pruritus, restlessness, blurred vision, wheezing and/or acute respiratory distress. Discontinue VONVENDI if hypersensitivity symptoms occur and administer appropriate emergency treatment.

Please see VONVENDI full Detailed Important Risk Information on page 9.
Please click here for VONVENDI full Prescribing Information.

Katie's menorrhagia is managed with 1 infusion of VONVENDI® [von Willebrand factor (Recombinant)][1,a]

PRE- AND POST-INFUSION VWF:RCo AND FVIII:C LEVELS[1,11]



Katie's baseline FVIII:C is 20 IU/dL; her hematologist decides an immediate rise in FVIII:C is not necessary.[1,a]

Katie receives 2360 IU of VONVENDI alone.[1,b]

20 hours later, factor levels were monitored. Katie's bleed was controlled with 1 infusion of VONVENDI alone.[1]

An increase in endogenous FVIII:C above 40 IU/dL can be expected in a majority of patients within 6 hours with a single infusion of VONVENDI depending on patient's baseline FVIII:C levels.[1]

[a] VONVENDI may be administered alone if a patient's baseline plasma FVIII:C level is ≥40% or if an immediate rise in FVIII levels is not necessary.[1]
[b] The recommended initial dose of VONVENDI is 40-50 IU/kg for minor bleeds and 50-80 IU/kg for major bleeds. Subsequent doses should range from 40-50 IU/kg (minor bleeds) and 40-60 IU/kg (major bleeds) every 8-24 hours, as clinically required. Katie receives 40 IU/kg (40 IU VONVENDI x 58.9 kg body weight).

Comprehensive dosing information can be found in the VONVENDI full Prescribing Information.

vonvendi
[von Willebrand factor (Recombinant)]

vonvendi
[von Willebrand factor (Recombinant)]

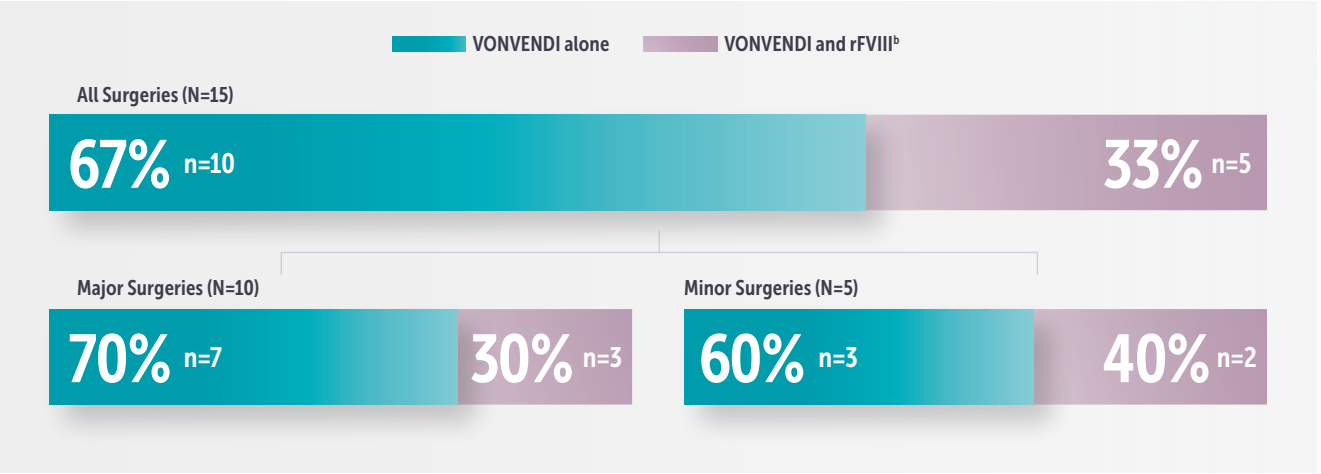
1 factor was all most patients needed in the surgical trial.[12,a]

A Phase 3 prospective, multicenter, open-label study assessed the efficacy and safety of VONVENDI with or without recombinant factor VIII (rFVIII) in adults (age 18 years and older) diagnosed with severe von Willebrand disease of all types undergoing elective surgical procedures.[1,12]

100% of patients had a mean overall hemostatic efficacy rating score of ≤2 (primary endpoint), assessed using a 4-point scale (Excellent=1, Good=2, Moderate=3, None=4) (90% CI, 81.9-100).[1]

Perioperative bleeding in most patients was managed by VONVENDI® [von Willebrand factor (Recombinant)] alone.[12]

10/15 PATIENTS RECEIVED NO CONCOMITANT rFVIII BEFORE, DURING, OR AFTER SURGERY[12]



[a] VONVENDI contains only trace amounts of rFVIII.
[b] Of the 5 patients who did receive concomitant rFVIII, 2 patients received a preoperative infusion (1 infusion each), 2 patients received a postoperative infusion (1 infusion each), and 1 patient received both one preoperative and six postoperative infusions.

Selected Important Risk Information

WARNINGS AND PRECAUTIONS (CONTINUED)

Neutralizing Antibodies (Inhibitors)

Inhibitors to VWF and/or factor VIII can occur. If the expected plasma levels of VWF activity (VWF:RCo) are not attained, perform an appropriate assay to determine if anti-VWF or anti-factor VIII inhibitors are present. Consider other therapeutic options and direct the patient to a physician with experience in the care of either VWD or hemophilia A.

In patients with high levels of inhibitors to VWF or factor VIII, VONVENDI therapy may not be effective and infusion of this protein may lead to severe hypersensitivity reactions. Since inhibitor antibodies can occur concomitantly with anaphylactic reactions, evaluate patients experiencing an anaphylactic reaction for the presence of inhibitors.

Please see VONVENDI full Detailed Important Risk Information on page 9.
Please click here for VONVENDI full Prescribing Information.

David: Surgical bleed*

61-year-old male
VWD type 2B
191 lb

"I was scared going into surgery, but my hematologist felt comfortable managing bleeding with VONVENDI. After I left the hospital, I was able to infuse VONVENDI every other day for two weeks at home."

–*David*

Undergoing right ankle fusion

History of ongoing hypertension

Medical history:
David was diagnosed with von Willebrand disease (VWD) type 2B at a hemophilia treatment center (HTC) as an adult shortly after his daughter was also diagnosed.[7] David began experiencing hypertension at the age of 43.

After diagnosis, David experienced several minor joint bleeds.[13] He has developed arthritis in lower joints and underwent a left knee replacement 5 years ago, prior to the availability of a recombinant von Willebrand factor (VWF).[1,13]

David's right ankle has begun causing him significant pain and based on imaging studies, his orthopedic surgeon recommends an ankle fusion.[14,15] His hemophilia treatment center team works closely with the surgical team at a partnering hospital to plan the surgery. Because David's FVIII:C is normal at 100 IU/dL, his hematologist decides to manage his surgery with VONVENDI.

*Photo and profile based on a hypothetical patient with VWD.

Selected Important Risk Information

ADVERSE REACTIONS

In clinical trials, the most common adverse reactions observed in ≥2% of subjects (n=80) were generalized pruritus, vomiting, nausea, dizziness, and vertigo.

One subject treated with VONVENDI in perioperative setting developed deep vein thrombosis after total hip replacement surgery.

Please see VONVENDI full Detailed Important Risk Information on page 9.
Please click here for VONVENDI full Prescribing Information.

David's hematologist chooses VONVENDI® [von Willebrand factor (Recombinant)] so he can dose VWF and recombinant factor VIII (rFVIII) independently[1,a]

PERIOPERATIVE BLEEDING MANAGEMENT FOR MAJOR SURGERY[1,12]

PREOPERATIVE

VWF:RCo – 19 IU/dL[8]
FVIII:C – 100 IU/dL

12-24 hours before surgery
Because David's baseline FVIII is already above the minimum target level for a major surgery (60 IU/dL), he does not receive a preoperative dose of VONVENDI.[1,b]

3 hours before surgery
His FVIII:C levels are assessed again, and are still at 100 IU/dL. VONVENDI is dosed alone within 1 hour of surgery.[1,c]

David receives 3500 IU VONVENDI based on baseline and target VWF:RCo levels for major surgery (target peak level: 100 IU/dL).[1,d]

During surgery
David does not require intraoperative infusion of VONVENDI during the 2-hour procedure.[1]

POSTOPERATIVE

VWF:RCo – 51 IU/dL[12]
FVIII:C – 120 IU/dL[12]

12 hours after surgery
David is monitored by his hematologist 12 hours after surgery and receives a dose of VONVENDI because his post-surgery VWF levels are nearing the minimum target.[1,e] He continues to be monitored at least once every 24 hours for 2 days after his surgery.[1]

VWF:RCo – 56 IU/dL[12]
FVIII:C – 123 IU dL

36 hours after surgery
David receives another infusion of VONVENDI and is dosed again 24 hours later before being discharged from the hospital. He is trained to infuse VONVENDI every other day at home, for a total of 2 weeks of treatment.[1,e]

[a] Dosing of VONVENDI, with or without rFVIII, should be based on patient need as determined by monitoring levels.
[b] VONVENDI may be administered 12-24 hours prior to surgery to allow endogenous FVIII levels to increase.
[c] FVIII:C level should be assessed within 3 hours prior to surgery to ensure minimum target levels are achieved; VONVENDI should be administered within 1 hour prior to surgery, either alone (if FVIII:C is at or greater than minimum target levels) or with rFVIII (if FVIII:C is below minimum target levels).
[d] Calculation of VONVENDI dose in IU is based on target peak VWF:RCo - baseline VWF:RCo x BW/IR, where IR is the incremental recovery as measured in the subject (assume an IR of 2.0 IU/dL per IU/kg if not available). David receives 3500 IU VONVENDI: (100 IU/dL-19 IU/dL) x 86.6 kg/2.
[e] Postoperatively, recommended minimum target plasma levels are as follows: Up to 72 hours post surgery: ≥30 IU/dL VWF:RCo and >30 IU/dL FVIII:C (minor surgery); >50 IU/dL VWF:RCo and FVIII:C (major surgery). After 72 hours post surgery: >30 IU/dL VWF:RCo and FVIII:C (major surgery). Dosing frequency should range between every 12 to 24 hours to every other day, for a minimum of 48 hours for minor and 72 hours for major surgery. The postoperative maintenance regimen should be individualized according to the pharmacokinetic results and intensity and duration of the hemostatic challenge.

VONVENDI promotes an increase in VWF activity levels (VWF:RCo), with a mean (SD) half-life of 19.1 (4.32) hours for PK_{80} and 22.6 (5.34) hours for PK_{50}.[1]

Comprehensive dosing information can be found in the VONVENDI full Prescribing Information.

vonvendi
[von Willebrand factor (Recombinant)]

VONVENDI® [von Willebrand factor (recombinant)] Important Information

Indications

VONVENDI [von Willebrand factor (recombinant)] is a recombinant von Willebrand factor (rVWF) indicated for use in adults (age 18 and older) diagnosed with von Willebrand disease (VWD) for:

- On-demand treatment and control of bleeding episodes
- Perioperative management of bleeding

Detailed Important Risk Information

CONTRAINDICATIONS

Do not use in patients who have had life-threatening hypersensitivity reactions to VONVENDI or its components (tri-sodium citrate-dihydrate, glycine, mannitol, trehalose-dihydrate, polysorbate 80, and hamster or mouse proteins).

WARNINGS AND PRECAUTIONS

Embolism and Thrombosis

Thromboembolic reactions, including disseminated intravascular coagulation, venous thrombosis, pulmonary embolism, myocardial infarction, and stroke, can occur, particularly in patients with known risk factors for thrombosis, including low ADAMTS13 levels. Monitor for early signs and symptoms of thrombosis such as pain, swelling, discoloration, dyspnea, cough, hemoptysis, and syncope, and institute prophylaxis measures against thromboembolism based on current recommendations.

In patients requiring frequent doses of VONVENDI in combination with recombinant factor VIII, monitor plasma levels for FVIII:C activity because sustained excessive factor VIII plasma levels can increase the risk of thromboembolic events.

One out of 80 subjects treated with VONVENDI in clinical trials developed proximal deep vein thrombosis in perioperative period after total hip replacement surgery.

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Neutralizing Antibodies (Inhibitors)

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In patients with high levels of inhibitors to VWF or factor VIII, VONVENDI therapy may not be effective and infusion of this protein may lead to severe hypersensitivity reactions. Since inhibitor antibodies can occur concomitantly with anaphylactic reactions, evaluate patients experiencing an anaphylactic reaction for the presence of inhibitors.

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One subject treated with VONVENDI in perioperative setting developed deep vein thrombosis after total hip replacement surgery.

Please click here for VONVENDI full Prescribing Information.

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