Von Willebrand factor (Vonvendi®)
EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO073

Description
Vonvendi is a recombinant von Willebrand factor indicated for use in adults diagnosed with von Willebrand disease for on-demand treatment and control of bleeding episodes, perioperative management, and routine prophylaxis in patients with severe Type 3 von Willebrand disease receiving on-demand therapy.

Length of Authorization
- Initial: 6 months (for on-demand and prophylaxis); 1 month (for perioperative)
- Renewal: 12 months

Quantity limits

Product Name	Indication/ FDA Labeled Dosing	Dosage Form	Quantity Limit
Vonvendi, von Willebrand factor (recombinant)	**On-demand treatment and control of bleeding episodes:** • *Minor:* Up to 50 IU/kg for the initial dose, subsequent doses of up to 50 IU/kg every eight to 24 hours as clinically required • *Major:* Up to 80 IU/kg for the initial dose, subsequent doses of up to 60 IU/kg every eight to 24 hours for approximately two to three days, as clinically required **Perioperative management of bleeding:** A dose may be given 12 to 24 hours prior to surgery to allow the endogenous factor VIII levels to increase to at least 30 IU/dL (minor surgery) or 60 IU/dL (major surgery) **Routine prophylaxis to reduce the frequency of bleeding episodes in patients with severe Type 3 VWD receiving on-demand therapy:** • For initiation, administer 40 to 60 IU/kg twice weekly • Adjust up to 60 IU/kg twice weekly if breakthrough bleeding occurs in joints or if severe bleeding occurs	650, 1300 IU	**On-demand treatment and control of bleeding episodes:** Up to the number of doses requested every 28 days **Perioperative management of bleeding:** Up to the number of doses requested every 28 days **Routine prophylaxis to reduce the frequency of bleeding episodes in patients with severe Type 3 VWD receiving on-demand therapy:** Up to the number of doses requested every 28 days

Initial Evaluation

I. **von Willebrand factor (Vonvendi)** may be considered medically necessary when the following criteria below are met:
   A. Treatment is prescribed by, or in consultation with, a hematologist; **AND**
   B. A diagnosis of von Willebrand disease (vWD) has been confirmed by blood coagulation and von Willebrand factor testing; **AND**
   C. Use is planned for one of the following indications:
      1. On-demand treatment and control of bleeding when one of the following is met:
         i. Member has severe von Willebrand disease (vWD); **OR**
         ii. Member has mild or moderate von Willebrand disease (vWD); **AND**
            a. The use of desmopressin is known or suspected to be ineffective or contraindicated; **OR**
      2. Perioperative management of bleeding; **OR**
      3. Routine prophylaxis and ALL are met:
         i. Confirmed severe type 3 VWD; **AND**
         ~~ii.~~ Currently receiving on-demand therapy.

II. Vonvendi is considered investigational when used for all other conditions.

Renewal Evaluation

I. Documentation of clinical benefit, including decreased incidence of bleeding episodes or stability of bleeding episodes relative to baseline

Supporting Evidence

I. Von Willebrand disease (vWD) is the most common of the inherited bleeding disorders. Although vWD is common, only a fraction of patients seeks out medical attention of bleeding symptoms due to the mild nature of the disease in many patients, and the lack of bleeding challenges.

II. There are three types of inherited vWD:
- Type 1 – The most common type that accounts for about 70% of cases. It reflects a quantitative deficiency of von Willebrand factor (vWF). The clinical presentation varies from mild to moderately severe.
- Type 2 – Accounts for 25-30% of cases and is characterized by several qualitative abnormalities of vWF (e.g. altered size rations or biologic properties).

- Type 3 – The most severe type of disease with very low or undetectable levels of vWF. Patients typically present with severe bleeding involving both the skin and mucous membrane surfaces and soft tissues and joints. Replacement therapy with vWF is usually required.

III. Choice of therapy begins with an accurate and complete diagnosis of vWD, plus patient-specific factors must be taken to account (e.g. history of bleeding, response to prior therapies).

IV. A trial of desmopressin (DDAVP) should be considered in all patients with type 1 and most with type 2, but not in patients with type 3 vWD. Typically, minor bleeding episodes can be treated with DDAVP without further therapeutic intervention. Major surgery typically requires replacement with vWF.

V. Patients with type 3 vWD, those with more severe type 1, and many of those with certain subtypes of type 2 disease often require replacement therapy with a vWF-containing product to control bleeding.

VI. The safety and efficacy of Vonvendi was established based on a series of 22 patients with vWD over the age of 18 years of age who experienced 192 bleeding episodes (mostly mucosal, seven major). Results showed the Vonvendi was highly effective in restoring hemostasis. Most episodes were treated with a single infusion.

VII. Use in routine prophylaxis was approved via a prospective, single arm, open-label, multicentered study that evaluated efficacy, safety, PK/PD of prophylactic treatment. Patients were age 18 years and older and diagnosed with vWD. Treatment groups included the prior on-demand (only received on-demand therapy) patients (n=13) and the switch (previously receiving prophylaxis therapy with plasma derived VWF (pdVWF)) patients (n=10). Treatment included rVWF 50 +/- 10 IU/kg twice weekly for the prior on-demand group and rVWF based on pdVWF weekly dose equivalent divided into 1-3 weekly infusions for the switch group for 12 months. Primary endpoint was the change in annualized bleeding rate (ABR) for spontaneous and non-traumatic bleeding events (BE) versus historical ABR.

VIII. The prior on-demand group had reduced ABR by 91.5% (mean ABR from 6.54 to 0.56) and the switch group had reduced ABR by 45% (mean ABR from 0.51 to 0.28) versus their historical ABR. No outstanding safety concerns noted outside of current data. Three serious AEs were reported that were considered unrelated to rVWF treatment (injuries due to a fall, 1 UTI, 1 related to rheumatoid arthritis comorbidity). There were no additional safety issues noted with the switch group. There were no binding or neutralizing antibodies found to either the rVWF or FVIII.

IX. Overall, the study demonstrated efficacy and safety for use of prophylaxis rVWF in patients who were only using on-demand therapy to reduce BEs. There was no significant efficacy for use in patients who were previously receiving other prophylactic therapy. However, given the rarity of this specific subtype and the lack of FDA-indicated products for prophylaxis use in this bleeding disorder, allowance in use of previously prophylaxis-treated patients provides access and other options in a limited treatment space.

Investigational or Not Medically Necessary Uses

I. There is no evidence to support the use of Vonvendi in any other condition.

References

1. Vonvendi® [Prescribing Information]. Westlake Village, CA: Baxalta US Inc; April 2022
2. National Hemophilia Foundation. MASAC Recommendations Concerning products Licensed for the Treatment of Hemophilia and Other Bleeding Disorders. Available from: https://www.hemophilia.org/Researchers-Healthcare-Providers/Medical-and-Scientific-Advisory-Council-MASAC/MASAC-Recommendations. Accessed July 5, 2019.
3. Nathan T. Connell, Veronica H. Flood, Romina Brignardello-Petersen, Rezan Abdul-Kadir, Alice Arapshian, Susie Couper, Jean M. Grow, Peter Kouides, Michael Laffan, Michelle Lavin, Frank W. G. Leebeek, Sarah H. O'Brien, Margareth C. Ozelo, Alberto Tosetto, Angela C. Weyand, Paula D. James, Mohamad A. Kalot, Nedaa Husainat, Reem A. Mustafa; ASH ISTH NHF WFH 2021 guidelines on the management of von Willebrand disease. Blood Adv 2021; 5 (1): 301–325. doi: https://doi.org/10.1182/bloodadvances.2020003264
4. Leebeek FWG, Peyvandi F, Escobar M, Tiede A, Castaman G, Wang M, Wynn T, Baptista J, Wang Y, Zhang J, Mellgård B, Özen G. Recombinant von Willebrand factor prophylaxis in patients with severe von Willebrand disease: phase 3 study results. Blood. 2022 Jul 14;140(2):89-98. doi: 10.1182/blood.2021014810. PMID: 35439298; PMCID: PMC9283967.
5. UpToDate, Inc. Treatment of von Willebrand disease. UpToDate [database online]. Last updated November 29, 2022.

Related Policies

Policies listed below may be related to the current policy. Related policies are identified based on similar indications, similar mechanisms of action, and/or if a drug in this policy is also referenced in the related policy.

Policy Name	Disease state
Factor VIII/VWF Complex (Alphanate®, Humate-P®, Wilate®)	Control and prevention of bleeding – hemophilia A
	Perioperative management – hemophilia A
	Control and prevention of bleeding – vWD
	Perioperative management – vWD

Policy Implementation/Update:

Action and Summary of Changes	Date
Added new indication and supportive evidence for prophylaxis use in patients with severe Type 3 vWD who are receiving on-demand therapy. Added new renewal approval duration of 12 months for prophylaxis use. Added related policies section.	03/2023
New policy created for von Willebrand factor (Vonvendi)	08/2019