

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Hematology – Vonvendi Management Medical Policy

- Vonvendi® (von Willebrand factor [recombinant] intravenous infusion – Baxalta)

REVIEW DATE: 12/04/2024

OVERVIEW

Vonvendi, a recombinant von Willebrand factor (VWF), is indicated for use in adults ≥ 18 years of age diagnosed with von Willebrand disease (VWD) for:¹

- **On-demand treatment and control** of bleeding episodes.
- **Perioperative management** of bleeding.
- **Routine prophylaxis to reduce the frequency of bleeding episodes in patients with severe Type 3 VWD** receiving on-demand therapy.

Disease Overview

VWD is an inherited bleeding disorder caused by a deficiency or impairment of a protein found in blood called VWF.³⁻⁶ VWF is a plasma protein with a dual role in hemostasis by mediating platelet adhesion at sites of vascular injury and by binding and stabilizing Factor VIII. The disease is rather common as it affects 1 in 100 people; both genders are impacted equally. Symptoms of VWD include mucocutaneous bleeding and excessive hemorrhage following invasive procedures; occasionally, soft tissue hematomas and joint bleeding may also occur. Women who have VWD may experience heavy menorrhagia or experience excessive bleeding at childbirth. Bleeding episodes may be life-threatening in patients with severe forms of VWD. VWD is classified into six types (1, 2A, 2B, 2M, 2N, and 3) according to distinct genotypic, clinical, and laboratory phenotypic characteristics. Type 1 VWD is the most common type (60% to 80% of patients) and represents a partial quantitative deficiency of VWF. Bleeding symptoms are generally mild to moderate. Type 2 VWD affects 15% to 30% of patients and consists of four disease subtypes (2A, 2B, 2M, and 2N) dependent on the specific gene mutation (e.g., decreased VWF-dependent platelet adhesion, decreased binding affinity for Factor VIII). This type is due to a qualitative VWF defect, and the bleeding is generally moderate, but can vary among patients. Type 3 VWD is uncommon (5% to 10% of patients) but is usually severe because it is due to a virtually complete deficiency of VWF. Many patients with VWD also have reduced Factor VIII levels. Treatment options for VWD include desmopressin either parenterally or by a highly concentrated nasal spray (Stimate), Vonvendi, or plasma-derived Factor VIII product that contain VWF.

Guidelines

The National Bleeding Disorders Foundation Medical and Scientific Advisory Council has guidelines for the treatment of hemophilia and other bleeding disorders (revised October 2024).³ Most patients with Type 1 VWD may be treated with a desmopressin product (DDAVP injection or Stimate nasal spray). Some patients with type 2A VWD may respond to DDAVP; a clinical trial with DDAVP should be performed to determine if DDAVP can be used for these particular patients. The guidelines recommend that both DDAVP injection and Stimate not be used in children aged < 2 years and in patients with VWD in whom desmopressin does not provide adequate VWF levels. Also, they should be used cautiously in pregnant women during labor and delivery. Use of plasma-derived VWF-containing Factor VIII concentrates that have VWF is recommended in certain types of VWD that do not respond to therapy with desmopressin (i.e., Type 2B VWD and Type 3 VWD). Also, plasma-derived Factor VIII concentrates that contain VWF (e.g., Alphanate, Humate-P, and Wilate) are recommended in Types 1, 2A, 2M, and 2N VWD who have become transiently unresponsive to DDAVP, as well as in surgical situations, especially in young children

< 2 years of age. Wilate is FDA-approved for routine prophylaxis in children \geq 6 years of age with VWD. Cryoprecipitate should not be utilized to treat patients with VWD except in life- and limb-threatening emergencies when VWD-containing factor VIII concentrate is not immediately available. Vonvendi is available to treat patients with Type 2B and Type 3 VWD; it can also be used in patients with Types 1, 2A, 2M, and 2N VWD who are not responsive to DDAVP and in children < 2 years of age, regardless of VWD type. Vonvendi is approved for use as routine prophylaxis only in patients with severe Type 3 VWD who were previously treated with VWF (recombinant or plasma-derived) on demand. It is produced in Chinese hamster ovary cells and it does not contain human or animal-derived proteins in its cell culture or in its final formulation (a third generation product). Vonvendi contains ultra-large VWF multimers, in addition to the high, medium, and low molecular weight VWF multimers normally found in plasma. Trace amounts of recombinant Factor VIII is in the product as well.

Dosing Considerations

Dosing of clotting factor concentrates is highly individualized. MASAC provides recommendations regarding doses of clotting factor concentrate in the home (2016).⁷ The number of required doses varies greatly and is dependent on the severity of the disorder and the prescribed regimen. Per MASAC guidance, patients on prophylaxis should also have a minimum of one major dose and two minor doses on hand for breakthrough bleeding in addition to the prophylactic doses used monthly. The guidance also notes that an adequate supply of clotting factor concentrate is needed to accommodate weekends and holidays. Therefore, maximum doses in this policy allow for prophylactic dosing plus three days of acute bleeding or perioperative management per 28 days. Doses exceeding this quantity will be reviewed on a case-by-case basis by a clinician.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage Vonvendi. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). Because of the specialized skills required for evaluation and diagnosis of patients treated with Vonvendi, as well as the monitoring required for adverse events and long-term efficacy, the agent is required to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Vonvendi is recommended for patients who meet the following criteria:

FDA-Approved Indication

1. **Von Willebrand Disease.** Approve for 1 year if the agent is prescribed by or in consultation with a hematologist.

Dosing. Approve the following dosing regimens (A, B, and/or C):

- A) **On demand treatment and control of bleeding episodes:** approve up to 900 IU/kg intravenously no more frequently than once every 28 days; AND/OR
- B) **Perioperative management:** approve up to 900 IU/kg intravenously no more frequently than once every 28 days; AND/OR

- C) Routine prophylaxis: approve up to 60 IU/kg intravenously no more frequently than twice weekly.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Vonvendi is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Vonvendi® intravenous infusion [prescribing information]. Lexington, MA: Baxalta; March 2023.
2. Gill JC, Castaman G, Windyga J, et al. Hemostatic efficacy, safety, and pharmacokinetics of a recombinant von Willebrand factor in severe von Willebrand disease. *Blood*. 2015;126(17):2038-2046.
3. Franchini M, Mannucci PM. Von Willebrand factor (Vonvendi®): the first recombinant product licensed for the treatment of von Willebrand disease. *Expert Rev Hematol*. 2016;9(9):825-830.
4. National Bleeding Disorders Foundation. MASAC (Medical and Scientific Advisory Council) recommendations concerning products licensed for the treatment of hemophilia and selected disorders of the coagulation system (October 2024). MASAC Document #290. Available at: <https://www.hemophilia.org/sites/default/files/document/files/MASAC-Products-Licensed.pdf>. Accessed on November 27, 2024.
5. Srivastava A, Santagostino E, Dougall A, et al, on behalf of the WFH guidelines for the management of hemophilia panelists and coauthors. WFH guidelines for the management of hemophilia, 3rd edition. *Haemophilia*. 2020;26 Suppl 6:1-158.
6. Connell NT, Flood VH, Brignardello-Petersen R, et al. ASH ISTH NHF WFH 2021 guidelines on the management of von Willebrand Disease. *Blood Adv*. 2021;5(1):301-325.
7. National Hemophilia Foundation. MASAC (Medical and Scientific Advisory Council) recommendations regarding doses of clotting factor concentrate in the home (Revised June 7, 2016). MASAC Document #242. Adopted on September 3, 2020. Available at: <https://www.hemophilia.org/sites/default/files/document/files/242.pdf>. Accessed on November 27, 2024.

HISTORY

| Type of Revision | Summary of Changes | Review Date |
|------------------|----------------------|-------------|
| Annual Revision | No criteria changes. | 11/08/2023 |
| Annual Revision | No criteria changes. | 12/04/2024 |