POLICY: Hematology – Vonvendi® (von Willebrand factor [recombinant] injection for intravenous use – Baxalta)

APPROVAL DATE: 09/11/2019

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; and 2) perioperative management of bleeding.[1]

Disease Overview

VWD is an inherited bleeding disorder caused by a deficiency or impairment of a protein found in blood called VWF. 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)[4] and represents a partial quantitative deficiency of VWF. Bleeding symptoms are generally mild to moderate.[5] 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)[4] but is usually severe because it is due to a virtually complete deficiency of VWF.[5] Many patients with VWD also have reduced Factor VIII levels. Treatment options for vonWillebrand disease include desmopressin either parenterally or by a highly concentrated nasal spray (Stimate), Vonvendi, or plasma-derived Factor VIII product that contain von Willebrand Factor.

Guidelines

The National Hemophilia Foundation Medical and Scientific Advisory Council has guidelines for the treatment of hemophilia and other bleeding disorders (revised April 2018).[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 deliver. 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 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. Alphanate, Humate-P, and Wilate are indicated for use in VWD; in certain patients Koāte®– DVI (antihemophilic Factor [plasma-derived] injection) may also be effective. Use of cryoprecipitate is not recommended as it has not undergone any viral attenuation steps. 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. It 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).[6] 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(s). 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.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Vonvendi is recommended for patients who meet 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 up to 900 IU/kg intravenously no more frequently than once every 28 days.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

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

REFERENCES

1. Vonvendi® injection for intravenous use [prescribing information]. Lexington, MA: Baxalta US; February 2019.
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. MASAC (Medical and Scientific Advisory Council) recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders (Revised April 2018). MASAC Document #253. Adopted on April 19, 2018. Available at: https://www.hemophilia.org/node/3675. Accessed on September 11, 2019.
5. Curnow J, Pasalic L, Favaloro EJ, et al. Treatment of von Willebrand disease. *Semin Thrombosis Hemostasis*. 2016;42(2):133-146.
6. 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 June 7, 2016. Available at: https://www.hemophilia.org/sites/default/files/document/files/242.pdf. Accessed on September 11, 2019.

HISTORY

Type of Revision	Summary of Changes	Approval Date
New policy	--	09/11/2019