Reference number(s)
4870-A

STANDARD MEDICARE PART B MANAGEMENT

WILATE (von Willebrand factor/coagulation factor VIII complex [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
   1. Wilate is indicated in children and adults with von Willebrand Disease (VWD) for:
      i. On-demand treatment and control of bleeding episodes
      ii. Perioperative management of bleeding
   2. Wilate is indicated in adolescents and adults with hemophilia A for:
      i. Routine prophylaxis to reduce the frequency of bleeding episodes
      ii. On-demand treatment and control of bleeding episodes

B. Compendial Use
   Acquired von Willebrand Syndrome

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. CRITERIA FOR INITIAL APPROVAL

A. Von Willebrand Disease
Authorization of 12 months may be granted for members with VWD when either of the following criteria is met:
1. Member has type 1, 2A, 2M, or 2N VWD and has had an insufficient response to desmopressin or a documented clinical reason for not using desmopressin (see Appendix B).
2. Member has type 2B or type 3 VWD.

B. Acquired von Willebrand Syndrome
Authorization of 12 months may be granted for treatment of acquired von Willebrand syndrome.

C. Hemophilia A
Authorization of 12 months may be granted for hemophilia A when the requested medication will be used for either of the following:
1. Member has mild disease (see Appendix A) and has had an insufficient response to desmopressin or a documented clinical reason for not using desmopressin (see Appendix B).
2. Member has moderate or severe disease (see Appendix A).

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Authorization for 12 months may be granted when all of the following criteria are met:
A. The member is currently receiving therapy with Wilate.
B. Wilate is being used to treat an indication enumerated in Section II.
C. The member is receiving benefit from therapy (e.g., reduced frequency or severity of bleeds).

Appendix A: Classification of Hemophilia by Clotting Factor Level (% Activity) and Bleeding Episodes

Severity	Clotting Factor Level % activity*	Bleeding Episodes
Severe	<1%	Spontaneous bleeding episodes, predominantly into joints and muscles Severe bleeding with trauma, injury or surgery
Moderate	1% to 5%	Occasional spontaneous bleeding episodes Severe bleeding with trauma, injury or surgery
Mild	6% to 40%	Severe bleeding with serious injury, trauma or surgery

*Factor assay levels are required to determine the diagnosis and are of value in monitoring treatment response.

Appendix B: Clinical Reasons For Not Utilizing Desmopressin in Patients with Hemophilia A and Type 1, 2A, 2M and 2N VWD
A. Age < 2 years
B. Pregnancy
C. Fluid/electrolyte imbalance
D. High risk for cardiovascular or cerebrovascular disease (especially the elderly)
E. Predisposition to thrombus formation
F. Trauma requiring surgery
G. Life-threatening bleed
H. Contraindication or intolerance to desmopressin
I. Severe type 1 von Willebrand disease
J. Stimate Nasal Spray is unavailable due to backorder/shortage issues (where applicable)

IV. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:
1. The prescribing information for Wilate.
2. The available compendium
    a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    b. Micromedex DrugDex
    c. American Hospital Formulary Service- Drug Information (AHFS-DI)
    d. Lexi-Drugs
    e. Clinical Pharmacology
3. The diagnosis, evaluation, and management of von Willebrand disease.
4. World Federation of Hemophilia (WFH) Guidelines for the Management of Hemophilia, 3rd edition.
5. MASAC recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders.

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Wilate are covered in addition to acquired von Willebrand syndrome.

V. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for using Wilate to treat von Willebrand syndrome can be found in the National Institutes of Health publication called the "Diagnosis, Evaluation, and Management of von Willebrand Disease". Type 2B and type 3 VWD does not respond consistently to DDAVP therapy and therefore DDAVP is not considered clinically useful in these patients.
The guideline from the National Bleeding Disorders Foundation (previously the National Hemophilia Foundation) also recommends using Wilate in VWD. Persons with type 2B and type 3 VWD, and those with type 1, 2A, 2M, and 2N who have been shown to be nonresponsive to DDAVP, should be treated with a factor VIII/VWF concentrate (such as Wilate) that is known to contain the higher molecular weight multimers of von Willebrand factor and that has been virally attenuated to eliminate transmission of HIV and hepatitis A, B, and C.

Support for using Wilate to treat acquired von Willebrand syndrome can be found in the National Institutes of Health publication called the "Diagnosis, Evaluation, and Management of von Willebrand Disease". The guideline indicates DDAVP and Wilate (VWF/FVIII) are first line therapy. If a patient has an inadequate response to DDAVP and VWF/FVIII concentrates, intravenous immunoglobulin given alone was effective in controlling bleeding and raising VWF:RCo activity.

Support for using Wilate to treat hemophilia A can be found in the National Bleeding Disorders Foundation (formerly the National Hemophilia Foundation) MASAC recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders. Recombinant factor VIII products are the recommended treatment of choice for patients with hemophilia A. A possible exception to this recommendation is a newly diagnosed individual, who should also consider with their healthcare providers initiating treatment with a plasma-derived FVIII / von Willebrand Factor (VWF) product.

IV. REFERENCES

1. Wilate [package insert]. Hoboken, NJ: Octapharma USA Inc.; November 2019.
2. National Institutes of Health. The diagnosis, evaluation, and management of von Willebrand disease. Bethesda, MD: US Dept of Health and Human Services, National Institutes of Health; 2007. NIH publication No. 08-5832.
3. Tiede A, Rand J, Budde U, et al. How I treat the acquired von Willebrand syndrome. *Blood*. 2011;117(25):6777-85.
4. Srivastava A, Santagostino E, Dougall A, et al. WFH Guidelines for the Management of Hemophilia, 3rd edition. *Haemophilia*. 2020 Aug;26 Suppl 6:1-158.
5. Federici A, Budde U, Castaman G, Rand J, Tiede A. Current diagnostic and therapeutic approaches to patients with acquired von Willebrand syndrome: a 2013 update. *Semin Thromb Hemost*. 2013;39(2):191-201.
6. National Hemophilia Foundation. MASAC recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders. Revised March 2022. MASAC Document #272. https://www.hemophilia.org/sites/default/files/document/files/272_Treatment.pdf. Accessed October 4, 2022.

7. National Hemophilia Foundation. MASAC recommendations regarding the treatment of von Willebrand disease. Revised February 2021. MASAC Document #266. https://www.hemophilia.org/sites/default/files/document/files/66.pdf. Accessed October 4, 2022.
8. Stimate [package insert]. King of Prussia, PA: CSL Behring LLC; June 2021.
9. Leissinger C, Carcao M, Gill JC, et al. Desmopressin (DDAVP) in the management of patients with congenital bleeding disorders. *Haemophilia*. 2014;20:158-167.