Disease Overview

Hemophilia A is an X-linked bleeding disorder primarily impacting males caused by a deficiency in Factor VIII.[20-24] In the US, the incidence of hemophilia A in males is 1:5,000 with an estimated 20,000 people in the US living with hemophilia A. The condition is characterized by bleeding in joints, either spontaneously or in a provoked joint. Bleeding can occur in many different body areas as well (e.g., muscles, central nervous system). The bleeding manifestations can lead to substantial morbidity such as hemophilic arthropathy. Disease severity is usually defined by the plasma levels or activity of Factor VIII classified as follows: severe (levels < 1% of normal), moderate (levels 1% to 5% of normal), and mild (levels > 5% to < 40% of normal); phenotypic expression may vary. Approximately 50% of patients with hemophilia A are categorized as having severe disease which may require routine prophylactic Factor VIII therapy.

VWD is a group of inherited bleeding disorders related to defects of von Willebrand Factor (vWF), which is needed to achieve hemostasis.[25-27] It occurs equally in males and females. The disease leads to bleeding from impaired platelet adhesion and aggregation, which may be accompanied by reduced levels of factor VIII. Mucous membrane and skin bleeding symptoms, as well as bleeding with surgical or other hematostatic challenges, may occur. The prevalence of the disease is approximately 1.3%. Pregnancy can increase vWF levels and confound the diagnosis. The three major subtypes of VWD include: partial quantitative vWF deficiency (type 1, 75% of patients); qualitative vWF deficiency (type 2, 25% of patients); and complete vWF deficiency (type 3, rare). Type 2 disease is further divided into four variants (2A, 2B, 2M, 2N) on the basis of the phenotype. In type 3 VWD, Factor VIII levels are usually very low. Acquired von Willebrand syndrome may result but is rare, occurring in fewer than one in 100,000 adults. The bleeding risk varies between modest increases in bleeding which occur only with procedures to a major risk of spontaneous hemorrhage. Approaches to the management of VWD involve increasing plasma concentrations of vWF through stimulation with desmopressin; replacing vWF by using human plasma-derived viral inactivated concentrates; and promoting hemostasis by use of hemostatic agents with mechanisms other than increasing vWF; and Vonvendi® (von Willebrand factor [recombinant] intravenous infusion). Regular prophylaxis is not frequently required.

Guidelines

Guidelines for hemophilia from the National Hemophilia Foundation (2022)[20] and the World Federation of Hemophilia (2020)[28] recognize the important role of Factor VIII products in the management of hemophilia A. Also, Factor VIII products that contain vWF have a role in the management of VWD.[23]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of the following Factor VIII products: Adynovate, Eloctate, Esperoct, Jivi, Advate, Afstyla, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, Xyntha, Hemofil M, Alphanate, Humate-P, Koate, and Wilate. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with recombinant Factor VIII products, 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

I. Coverage of Adynovate, Eloctate, Esperoct, Jivi, Advate, Afstyla, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, and Xyntha is recommended in those who meet the following criteria.

FDA-Approved Indication

1. **Hemophilia A.** Approve the requested agent for 1 year if the agent is prescribed by or in consultation with a hemophilia specialist.

II. Coverage of Hemofil M, Alphanate, Humate-P, Koate, and Wilate is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Hemophilia A.** Approve the requested agent for 1 year if the agent is prescribed by or in consultation with a hemophilia specialist.

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

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of the cited Factor VIII products 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. Adynovate® intravenous infusion [prescribing information]. Lexington, MA: Baxalta; June 2021.
2. Eloctate® intravenous infusion [prescribing information]. Waltham, MA: Bioverativ; December 2020.
3. Jivi® intravenous infusion [prescribing information]. Whippany, NJ: Bayer; August 2018.
4. Esperoct® intravenous infusion [prescribing information]. Plainsboro, NJ: Novo Nordisk; August 2022.
5. Advate® intravenous infusion [prescribing information]. Westlake Village, CA: Baxalta/Shire; December 2018.
6. Kovaltry® intravenous infusion [prescribing information]. Whippany, NJ: Bayer; December 2022.
7. Afstyla® intravenous infusion [prescribing information]. Kankakee, IL: CSL Behring; April 2021.
8. Kogenate® FS lyophilized powder for reconstitution for intravenous infusion [prescribing information]. Whippany, NJ: Bayer; December 2019.
9. Novoeight® intravenous infusion [prescribing information]. Plainsboro, NJ: Novo Nordisk; July 2020.
10. Nuwiq® intravenous infusion [prescribing information]. Paramus, NJ: Octapharma; June 2021.
11. Recombinate™ intravenous infusion [prescribing information]. Lexington, MA: Baxalta; June 2021.
12. Xyntha® intravenous infusion [prescribing information]. Philadelphia, PA: Wyeth/Pfizer; July 2022.
13. Xyntha® Solofuse™ intravenous infusion [prescribing information]. Philadelphia, PA: Wyeth/Pfizer; July 2022.
14. Hemofil® M intravenous infusion [prescribing information]. Lexington, MA: Baxalta; June 2018.
15. Alphanate® intravenous infusion [prescribing information]. Los Angeles, CA: Grifols; March 2021.
16. Humate-P® intravenous infusion [prescribing information]. Kankakee, IL: CSL Behring; June 2020.
17. Koāte® intravenous infusion [prescribing information]. Fort Lee, NJ and Research Triangle Park, NC: Kedrion and Grifols; June 2018.
18. Wilate® intravenous infusion [prescribing information]. Hoboken, NJ: Octapharma; September 2019.
19. Altuviiio™ intravenous infusion [prescribing information]. Waltham, MA: Bioverativ/Sanofi; February 2023.
20. National Hemophilia Foundation. Medical and Scientific Advisory Council (MASAC) recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders (Revised March 2022). MASAC document #272. Available at: https://www.hemophilia.org/healthcare-professionals/guidelines-on-care/masac-documents/masac-document-272-masac-recommendations-concerning-products-licensed-for-the-treatment-of-hemophilia-and-other-bleeding-disorders. Accessed on March 13, 2023.
21. Mancuso ME, Mahlangu JN, Pipe SW. The changing treatment landscape in haemophilia: from standard half-life clotting factor concentrates to gene editing. *Lancet*. 2021;397:630-640.
22. Croteau SE. Hemophilia A/B. *Hematol Oncol Clin North Am*. 2022;36(4):797-812.
23. Franchini M, Mannucci PM. The more recent of hemophilia treatment. *Semin Thromb Hemost*. 2022;48(8):904-910.

24. Peyvandi F, Garagiola I, Young G. The past and future of haemophilia: diagnosis, treatments and its complications. *Lancet*. 2016;388(10040):187-197.
25. Neff AT, Sidonio RF. Management of VWD. *Hematology Am Soc Hematol Educ Program*. 2014;(1):536-541.
26. Nichols WL, Hultin MB, James AH, et al. von Willebrand disease (vWD): evidence-based diagnosis and management guidelines, the National Heart, Lung, and Blood Institute (NHLBI) Expert Panel Report (USA). *Haemophilia*. 2008;14(2):171-232.
27. Favaloro EJ, Bodo I, Israels SJ, Brown SA. Von Willebrand disease and platelet disorders. *Hemophilia*. 2014;20(Suppl 4):59-64.
28. Srivastava A, Santagostino E, Dougall A, on behalf of the WFH guidelines for the management of hemophilia panelists and co-authors. Guidelines for the management of hemophilia, 3rd edition. *Haemophilia*. 2020;26(Suppl 6):1-158.