PRIOR AUTHORIZATION POLICY

POLICY: Hemophilia – Factor VIII Products

Extended Half-Life Products

- Adynovate® (Antihemophilic Factor PEGylated intravenous infusion – Baxalta/Takeda)
- Eloctate® (Antihemophilic Factor Fc fusion protein intravenous infusion – Bioverativ/Sanofi)
- Esperoct® (Antihemophilic factor glycopegylated intravenous infusion – Novo Nordisk)
- Jivi® (Antihemophilic Factor PEGylated-aucl intravenous infusion – Bayer HealthCare)

Standard Half-Life Products

- Advate® (Antihemophilic Factor intravenous infusion – Baxalta/Takeda)
- Afstyla® (Antihemophilic Factor single chain intravenous infusion – CSL Behring)
- Kogenate® FS (Antihemophilic Factor intravenous infusion – Bayer HealthCare)
- Kovaltry® (Antihemophilic Factor intravenous infusion – Bayer HealthCare)
- Novoeight® (Antihemophilic Factor intravenous infusion – Novo Nordisk)
- Nuwiq® (Antihemophilic Factor intravenous infusion – Octapharma)
- Recombinate® (Antihemophilic Factor intravenous infusion – Baxalta/Takeda)
- Xyntha®/Xyntha® Solofuse™ (Antihemophilic Factor intravenous infusion, plasma/albumin-free – Wyeth/Pfizer)

Plasma-Derived Standard Half-Life Products without Von Willebrand Factor

- Hemofil® M (Antihemophilic Factor intravenous infusion – Baxalta/Takeda)

Plasma-Derived Standard Half-Life Products with Von Willebrand Factor

- Alphanate® (Antihemophilic Factor/von Willebrand Factor Complex [human] intravenous infusion – Grifols)
- Humate-P® (Antihemophilic Factor/von Willebrand Factor Complex intravenous infusion – CSL Behring)
- Koāte® (Antihemophilic Factor intravenous infusion – Grifols/Kedrion Biopharma)
- Wilate® (von Willebrand Factor/Coagulation Factor VIII Complex intravenous infusion – Octapharma)

REVIEW DATE: 02/28/2024

OVERVIEW

For the **management of hemophilia A**, many recombinant Factor VIII products are available, including extended half-life products[1-4] (Adynovate, Eloctate, Esperoct, and Jivi) as well as standard half-life products (Advate, Afstyla, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, and Xyntha).[5-13] In general, these products are utilized in various clinical scenarios in the management of patients with hemophilia A. Several standard half-life Factor VIII plasma-derived products are available. Hemofil M is a plasma-derived standard half-life product that does not contain substantial amounts of von Willebrand Factor which is indicated for use in the management of hemophilia A.[14] Plasma-derived Factor VIII products that contain von Willebrand Factor include Alphanate, Humate P, Koate, and Wilate.[15-18] Alphanate, Humate P, and Wilate are indicated for use in clinical scenarios for the management of hemophilia A, as well as in patients with von Willebrand disease (VWD).[15,16,18] Wilate is the only agent FDA-approved for use in routine prophylaxis in children 6 years of age and older and adults with VWD.[18] However, the other agents have been used in this clinical scenario as well.[29] Koate is indicated for the control and prevention of bleeding

episodes or in order to perform emergency elective surgery in patients with hemophilia A.[17] This policy does not include Altuviiio™ (antihemophilic factor [recombinant] Fc-VWF-XTEN fusion protein-ehtl intravenous injection).[19]

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 and Koate 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.

III. Coverage of Alphanate, Humate-P, 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/Takeda; August 2023.
2. Eloctate® intravenous infusion [prescribing information]. Waltham, MA: Bioverativ/Sanofi; May 2023.
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]. Lexington, MA: Baxalta/Takeda; March 2023.
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/Takeda; March 2023.
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/Takeda; March 2023.
15. Alphanate® intravenous infusion [prescribing information]. Los Angeles, CA: Grifols; November 2022.
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; December 2023.
19. Altuviiio™ intravenous infusion [prescribing information]. Waltham, MA: Bioverativ/Sanofi; March 2023.
20. National Bleeding Disorders Foundation. Medical and Scientific Advisory Council (MASAC) recommendations concerning products licensed for the treatment of hemophilia selected disorders of the coagulation system (Revised August 19, 2023 and endorsed on August 20, 2023). MASAC document #280. Available at: https://www.hemophilia.org/sites/default/files/document/files/MASAC-Products-Licensed.pdf. Accessed on February 22, 2024.
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.
29. Franchini M, Seidizadeh O, Mannucci PM. Prophylactic management of patients with von Willebrand disease. *Ther Adv Hematol*. 2021;12:1-12.