PreferredOne®

PRIOR AUTHORIZATION POLICY

POLICY: Hemophilia – Factor VIII Products

Extended Half-Life Products

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

Standard Half-Life Products

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

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

- Hemofil® M (Antihemophilic Factor injection –Baxalta)
- Monoclate-P® (Antihemophilic Factor injection – CSL Behring)

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

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

REVIEW DATE: 03/03/2021

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, Helixate, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, and Xyntha).[5-16] 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 and Monoclate P are plasma-derived standard half-life products that do not contain substantial amounts of von Willebrand Factor which are indicated for use in the management of hemophilia A.[17,18] Plasma-derived Factor VIII products that contain von Willebrand Factor include Alphanate, Humate P, Koate, and Wilate.[19-22] 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.[19,20, 22] Koate is indicated for the control and prevention of bleeding episodes or in order to perform emergency elective surgery in patients with hemophilia A.[21]

Disease Overview

Hemophilia A is an X-linked bleeding disorder caused by a deficiency in Factor VIII.[23-25] 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. Sometimes the disorder is caused by a spontaneous genetic mutation. Males primarily have the disorder and most times females are asymptomatic carriers. The condition is characterized by bleeding in joints, either spontaneously or in a provoked joint. Bleeding can occur in many different body areas (e.g., muscles, central nervous system, gastrointestinal). Hemarthrosis is the main sign of hemophilia in older children and adults. In newborns and toddlers, bleeding in the head (intracranial hemorrhage and extracranial hemorrhage), bleeding from circumcision, and in the oral cavity are more common. The bleeding manifestations can lead to substantial morbidity, as well as mortality, if not properly treated. Disease severity is usually defined by the plasma levels of Factor VIII and have been classified as follows: severe (levels less than 1% of normal [normal plasma levels are 50 to 100 U/dL]), moderate (levels 1% to 5% of normal), and mild (levels > 5%); phenotypic expression may also vary. Approximately 25% to 30% of patients with hemophilia A have severe deficiency whereas 3% to 13% of patients have moderate to mild deficiency. Diagnoses can be substantially delayed, especially in patients with mild disease, as bleeding may not clinically occur. Higher doses than that typically used for the uses of standard half-life products can be given if the patient develops an inhibitor, which develop in approximately 25% of patients.[26]

Von Willebrand disease is a group of inherited bleeding disorders related to defects of von Willebrand Factor (vWF), which is needed to achieve hemostasis.[27-29] 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 von Willebrand disease 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 von Willebrand disease, 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 von Willebrand disease 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] injection for intravenous use). Regular prophylaxis is not frequently required.

Guidelines

Guidelines for hemophilia from the National Hemophilia Foundation (2020)[23] and the World Federation of Hemophilia (2020)[30] recognize the important role of Factor VIII products in the management of hemophilia A in patients. Also, Factor VIII products that contain vWF have a role in the management of von Willebrand disease.[23]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of the following Factor VIII products: Adynovate, Eloctate, Esperoct, Jivi, Advate, Afstyla, Helixate FS, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, Xyntha, Hemofil M, Monoclate P, 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.

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Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

I. Coverage of Adynovate, Eloctate, Esperoct, Jivi, Advate, Afstyla, Helixate FS, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, and Xyntha 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.

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

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 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® lyophilized powder for solution for intravenous injection [prescribing information]. Lexington, MA: Baxalta; May 2018.
2. Eloctate® lyophilized powder for solution for intravenous injection [prescribing information]. Waltham, MA: Bioverativ; September 2019.
3. Jivi® lyophilized powder for solution for intravenous use [prescribing information]. Whippany, NJ: Bayer HealthCare; August 2018.
4. Esperoct® lyophilized powder for solution for intravenous use [prescribing information]. Plainsboro, NJ: Novo Nordisk; October 2019.
5. Advate® lyophilized powder for reconstitution for intravenous injection [prescribing information]. Westlake Village, CA: Baxalta/Shire; December 2018.
6. Kovaltry® lyophilized powder for solution for intravenous injection [prescribing information]. Whippany, NJ: Bayer HealthCare; March 2016.
7. Afstyla® lyophilized powder for solution for intravenous injection [prescribing information]. Kankakee, IL: CSL Behring; April 2020.
8. Helixate® FS lyophilized powder for reconstitution for intravenous use [prescribing information]. Kankakee, IL and Whippany, NJ: CSL Behring and Bayer HealthCare; May 2016.
9. Kogenate® FS lyophilized powder for reconstitution for intravenous use [prescribing information]. Whippany, NJ: Bayer HealthCare; May 2016.
10. Kogenate® FS lyophilized powder for reconstitution with vial adapter for intravenous use [prescribing information]. Whippany, NJ: Bayer HealthCare; December 2019.
11. Kogenate® FS lyophilized powder for reconstitution with BIO-SET® for intravenous use [prescribing information]. Whippany, NJ: Bayer HealthCare; May 2016.

12. Novoeight® lyophilized powder for solution for intravenous injection [prescribing information]. Plainsboro, NJ: Novo Nordisk; November 2018.
13. Nuwiq® lyophilized powder solution for intravenous injection [prescribing information]. Hoboken, NJ: Octapharma; July 2017.
14. Recombinate™ lyophilized powder for reconstitution for injection [prescribing information]. Lexington, MA: Baxalta; June 2018.
15. Xyntha® lyophilized powder for solution intravenous injection [prescribing information]. Philadelphia, PA: Wyeth Pharmaceuticals (a subsidiary of Pfizer); Augus 2020.
16. Xyntha® Solofuse™ lyophilized powder for solution in prefilled dual chamber syringe for intravenous injection [prescribing information]. Philadelphia, PA: Wyeth Pharmaceuticals (a subsidiary of Pfizer); August 2020.
17. Hemofil® M for intravenous use [prescribing information]. Lexington, MA: Baxalta; June 2018.
18. Monoclate-P® for intravenous use [prescribing information]. Kankakee, IL: Aventis Behring; February 2014.
19. Alphanate® for intravenous injection [prescribing information]. Los Angeles, CA: Grifols; June 2018.
20. Humate-P® lyophilized powder for reconstitution for intravenous use [prescribing information]. Kankakee, IL: CSL Behring; September 2017.
21. Koāte for intravenous injection [prescribing information]. Fort Lee, NJ and Research Triangle Park, NC: Kedrion Biopharmaand Grifols; June 2018.
22. Wilate® lyophilized powder for solution for intravenous injection [prescribing information]. Hoboken, NJ: Octapharma; September 2019.
23. National Hemophilia Foundation. Medical and Scientific Advisory Council (MASAC) recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders (Revised August 2020). MASAC document #263. Available at: 263_treatment.pdf (hemophilia.org). Accessed on February 22, 2021.
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25. Berntorp E, Shapiro. Modern haemophilia care. *Lancet*. 2012;379:1447-1456.
26. Valentino LA, Kempton CL, Kruse-Jarres R, et al, on behalf of the International Immune Tolerance Induction Study Investigators. US guidelines for immune tolerance induction in patients with haemophilia a and inhibitors. *Haemophilia*. 2015;21(5):559-567.
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28. 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.
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30. 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. Available at: WFH Guidelines for the Management of Hemophilia, 3rd edition (wiley.com). Accessed on February 13, 2021.

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PO Box 59052
Minneapolis, MN 55459-0052
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Fax: 763.847.4010
customerservice@preferredone.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, a Grievance Specialist is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1-800-368-1019, 800-537-7697 (TDD)

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Fax: 763.847.4010
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U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1-800-368-1019, 800-537-7697 (TDD)

Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html.

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