VENTURA COUNTY
HEALTH CARE PLAN

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Hemophilia – Factor VIII Products Utilization Management Medical Policy

Extended Half-Life Products

- Adynovate® (Antihemophilic Factor PEGylated intravenous infusion – Baxalta)
- Eloctate® (Antihemophilic Factor Fc fusion protein intravenous infusion – Bioverativ)
- 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)
- Afstyla® (Antihemophilic Factor single chain intravenous infusion – CSL Behring)
- Helixate® FS (Antihemophilic Factor intravenous infusion – Bayer HealthCare/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)
- 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)
- Monoclate-P® (Antihemophilic Factor intravenous infusion – CSL Behring)

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 for intravenous infusion – Octapharma)

REVIEW DATE: 03/09/2022

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 (VWD).[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]

VWD 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 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 (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 VWD.[23]

POLICY STATEMENT

Prior Authorization is recommended for medical 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. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. 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). 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, Helixate FS, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, and Xyntha is recommended in those who meet the following criteria.

FDA-Approved Indication

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

Dosing. Approve one of the following dosing regimens (A or B):

A) For Adynovate, Eloctate, Esperoct, and Jivi approve the following dosing regimens (i, ii, and/or iii):
- **i.** Routine prophylaxis: approve up to 100 IU per kg intravenously no more frequently than twice weekly; AND/OR
- **ii.** On-demand treatment and control of bleeding episodes: approve up to 65 IU per kg intravenously no more frequently than once every 8 hours for up to 10 days per episode; AND/OR
- **iii.** Perioperative management: approve up to 65 IU per kg intravenously no more frequently than once every 6 hours for up to 10 days per procedure; OR

B) For Advate, Afstyla, Helixate FS, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, and Xyntha approve the following dosing regimens (i, ii, iii, and/or iv):
- **i.** Routine prophylaxis: approve up to 60 IU per kg intravenously no more frequently than every other day (three or four times weekly); AND/OR
- **ii.** On-demand treatment and control of bleeding episodes: approve up to 50 IU per kg intravenously no more frequently than once every 6 hours for up to 10 days per episode; AND/OR
- **iii.** Perioperative management: approve up to 60 IU per kg intravenously no more frequently than once every 6 hours for up to 10 days per procedure; AND/OR
- **iv.** Immune tolerance therapy (also known as immune tolerance induction): approve up to 200 IU per kg intravenously no more frequently than once daily.

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

FDA-Approved Indications

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1. Hemophilia A. Approve Hemofil M, Monoclate-P, Koate, Alphanate, Humate P, and Wilate for 1 year if the agent is prescribed by or in consultation with a hemophilia specialist.

Dosing. Approve the following dosing regimens:

A) Routine prophylaxis: approve up to 50 IU per kg intravenously no more frequently than every other day (three or four times weekly); AND/OR

B) On-demand treatment and control of bleeding episodes and perioperative management: approve up to 50 IU per kg intravenously no more frequently than once every 6 hours for up to 10 days per episode or procedure; AND/OR

C) Immune tolerance therapy (also known as immune tolerance induction): approve up to 200 IU per kg intravenously no more frequently than once daily.

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2. Von Willebrand Disease. Approve Alphanate, Humate P, and Wilate for 1 year if the agent is prescribed by or in consultation with a hemophilia specialist.

Dosing. On-demand treatment and control of bleeding episodes and perioperative management: approve up to 80 IU VWF:RCo per kg intravenously no more frequently than once every 8 hours for up to 10 days per episodes or procedure.

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; October 2019.
5. Advate® intravenous infusion [prescribing information]. Westlake Village, CA: Baxalta/Shire; December 2018.
6. Kovaltry® intravenous infusion [prescribing information]. Whippany, NJ: Bayer; October 2021.
7. Afstyla® intravenous infusion [prescribing information]. Kankakee, IL: CSL Behring; April 2021.
8. Helixate® FS intravenous infusion [prescribing information]. Kankakee, IL and Whippany, NJ: CSL Behring and Bayer; May 2016.
9. Kogenate® FS lyophilized powder for reconstitution for intravenous infusion [prescribing information]. Whippany, NJ: Bayer; May 2016.
10. Kogenate® FS lyophilized powder for reconstitution with vial adapter for intravenous infusion [prescribing information]. Whippany, NJ: Bayer; December 2019.
11. Kogenate® FS lyophilized powder for reconstitution with BIO-SET® for intravenous infusion [prescribing information]. Whippany, NJ: Bayer; May 2016.
12. Novoeight® lyophilized powder for solution for intravenous infusion [prescribing information]. Plainsboro, NJ: Novo Nordisk; July 2020.
13. Nuwiq® intravenous infusion [prescribing information]. Paramus, NJ: Octapharma; September 2020.
14. Recombinate™ lyophilized powder for reconstitution for intravenous infusion [prescribing information]. Lexington, MA: Baxalta; June 2018.
15. Xyntha® lyophilized powder for solution intravenous infusion [prescribing information]. Philadelphia, PA: Wyeth/Pfizer; August 2020.
16. Xyntha® Solofuse™ lyophilized powder for solution in prefilled dual chamber syringe for intravenous infusion [prescribing information]. Philadelphia, PA: Wyeth/Pfizer; August 2020.
17. Hemofil® M intravenous infusion [prescribing information]. Lexington, MA: Baxalta; June 2018.
18. Monoclate-P® intravenous infusion [prescribing information]. Kankakee, IL: Aventis Behring; February 2014.
19. Alphanate® for intravenous infusion [prescribing information]. Los Angeles, CA: Grifols; March 2021.
20. Humate-P® intravenous infusion [prescribing information]. Kankakee, IL: CSL Behring; June 2020.

21. Koāte intravenous infusion [prescribing information]. Fort Lee, NJ and Research Triangle Park, NC: Kedrion Biopharma and Grifols; June 2018.
22. Wilate® intravenous infusion [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 March 3, 2022.
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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.
27. Neff AT, Sidonio RF. Management of VWD. *Hematology Am Soc Hematol Educ Program*. 2014;(1):536-541.
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.
29. Favaloro EJ, Bodo I, Israels SJ, Brown SA. Von Willebrand disease and platelet disorders. *Hemophilia*. 2014;20(Suppl 4):59-64.
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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	03/03/2021
Annual Revision	No criteria changes.	03/09/2022