UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Hemophilia – Factor VIII Products Utilization Management Medical Policy

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 for intravenous infusion – Octapharma)

REVIEW DATE: 02/11/2026; selected revision 07/22/2026

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 adult and pediatric patients with VWD.[18] However, the other agents have been used in this

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clinical scenario as well.[27] 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 involve Altuviiio® (antihemophilic factor [recombinant] Fc-VWF-XTEN fusion protein-ehtl intravenous infusion).[19] Many other agents are also involved in the management of hemophilia A.[20]

Disease Overview

Hemophilia A is an X-linked bleeding disorder primarily impacting males caused by a deficiency in Factor VIII.[21-23] The prevalence of hemophilia A in males is 1:5,000 live births.[23] The condition is characterized by bleeding in joints, either spontaneously or in a provoked joint by trauma.[21-23] 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.[21-23] Disease severity is usually defined by the plasma levels or activity of Factor VIII. Normal plasma levels of Factor VIII range from 50% to 150%.[22] The disease is classified based on reduced levels. Mild, moderate, and severe hemophilia A is characterized by Factor IX levels ranging from 6% up to 49%, 1% up to 5%, and < 1%, respectively.[22] Approximately 60% of patients with hemophilia A are categorized as having severe disease.

VWD is a group of inherited bleeding disorders related to defects of von Willebrand Factor (vWF), which is needed to achieve hemostasis.[24-26] It occurs equally in males and females; it impacts around 1% of the population. The disease is associated with mucous membrane bleeding, excessive bruising, and bleeding from cuts. Excessive bleeding may result following invasive dental work, during surgical procedures, and following an accident or injury. Heavy menstrual bleeding is often a major symptoms among women. Also, women who have VWD are at risk of postpartum hemorrhage.[26] Types 1 and 3 disease are due to a quantitative vWF deficiency and Type 2 disease represents a qualitative vWF deficiency.[24] The 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, promoting hemostasis by use of hemostatic agents with mechanisms other than increasing vWF, and Vonvendi® (von Willebrand factor [recombinant] intravenous infusion). Regular prophylaxis can be used for some patients.[24-26]

Guidelines

Guidelines for hemophilia from the National Bleeding Disorders Foundation (2024)[20] and the International Society on Thrombosis and Haemostasis (2024)[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 as cited by the American Society of Hematology, the International Society of Thrombosis and Hemostasis, the National Hemophilia Foundation, and the World Federation of Hemophilia 2021 guidelines for the management of von Willebrand disease.[25] The National Hemophilia Foundation has also adapted these guidelines.[26]

POLICY STATEMENT

Prior Authorization is recommended for medical 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. 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.

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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

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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, iii, and/or iv):
- **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; 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.

B) For Advate, Afstyla, 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 and Koate 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 the following dosing regimens (A, B, and/or C):

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

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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.

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

FDA-Approved Indications

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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 the following dosing regimens (A, B, and/or C):
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 the requested agent for 1 year if the agent is prescribed by or in consultation with a hemophilia specialist.

Dosing. Approve the following dosing regimens (A and/or B):
A) On-demand treatment and control of bleeding episodes and perioperative management: approve up to 80 IU VWF:RCo (Von Willebrand Factor activity as measured with the Ristocetin cofactor assay) per kg intravenously no more frequently than once every 8 hours for up to 10 days per episode or procedure; AND/OR
B) Routine prophylaxis: approve up to 100 IU VWF:RCo per kg intravenously no more frequently than once every 2 days.

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; October 2025.
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; July 2024.
5. Advate® intravenous infusion [prescribing information]. Lexington, MA: Baxalta/Takeda; March 2025.
6. Kovaltry® intravenous infusion [prescribing information]. Whippany, NJ: Bayer; December 2022.
7. Afstyla® intravenous infusion [prescribing information]. Kankakee, IL: CSL Behring; June 2023.

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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; December 2024.
11. Recombinate™ intravenous infusion [prescribing information]. Cambridge, MA: Baxalta/Takeda; March 2025.
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; January 2022.
18. Wilate® intravenous infusion [prescribing information]. Paramus, NJ: Octapharma; July 2026.
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21. Konkle BA, Nakaya Fletcher S. Hemophilia A. 2000 Sep 21 [Updated 2025 Aug 7]. In: Adam MP, Bick S, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2026.
22. National Bleeding Disorders Foundation. Hemophilia A: An overview of symptoms, genetics, and treatments to help you understand hemophilia A. Available at: https://www.bleeding.org/bleeding-disorders-a-z/types/hemophilia-a. Accessed on April 5, 2025.
23. Chowdary P, Carcao M, Kenet G, Pipe SW. Haemophilia. *Lancet*. 2025;405:736-750.
24. Connell NT. Treatment of von Willebrand disease. *Blood Adv*. 2026;10(3):794-801.
25. ASH ISTH NHF WFH 2021 guidelines on the management of von Willebrand disease. *Blood Adv*. 2021;5(1):301-325.
26. MASAC recommendations regarding the treatment of von Willebrand Disease. MASAC recommendation # 266. Adopted March 4, 2021. Available at: https://www.hemophilia.org/sites/default/files/document/files/266.pdf. Accessed on February 9, 2026.
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28. Rezende SM, Neumann I, Angchaisuksiri P, et al. International Society on Thrombosis and Haemostasis clinical practice guideline for the treatment of congenital hemophilia A and B based on the Grading of Recommendations Assessment, Development, and Evaluation methodology. *J Thromb Haemost*. 2024;22:2629-2652.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	02/28/2024
Selected Revision	**Hemophilia A:** Added **Dosing** for Adynovate, Eloctate, Esperoct, and Jivi for immune tolerance therapy (also known as immune tolerance induction).	11/13/2024
Annual Revision	No criteria changes.	02/19/2025
Annual Revision	No criteria changes.	02/11/2026
Selected Revision	**Von Willebrand Disease:** Dosing for routine prophylaxis was changed from 40 IU to 100 IU per the provided regimen.	07/22/2026

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