POLICY Document for FACTOR VIII CONCENTRATES

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

Hemophiliaq CAREFIRST: EXCEPTIONS CRITERIA

HEMOPHILIA A

PREFERRED PRODUCTS: ELOCTATE, HEMLIBRA, XYNTHA/SOLOFUSE, NUWIQ

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the Factor VIII products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred products and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members who are requesting treatment with the targeted products

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Factor VIII Products

	Product(s)
Preferred*	• **Eloctate** (antihemophilic factor [recombinant]) • **Hemlibra** (emicizumab-kxwh) • **Nuwiq** (antihemophilic factor [recombinant]) • **Xyntha (including Solofuse)** (antihemophilic factor [recombinant])
Targeted	• **Advate** (antihemophilic factor [recombinant]) • **Adynovate** (antihemophilic factor [recombinant]) • **Afstyla** (antihemophilic factor [recombinant]) • **Altuviiio** (antihemophilic factor [recombinant]) • **Esperoct** (antihemophilic [recombinant]) • **Jivi** (antihemophilic factor [recombinant]) • **Kogenate FS** (antihemophilic factor [recombinant]) • **Kovaltry** (antihemophilic factor [recombinant]) • **Novoeight** (antihemophilic factor [recombinant]) • **Recombinate** (antihemophilic factor [recombinant]) • **Roctavian** (Valoctogene roxaparvovec-rvox)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred product.

Coverage for the targeted product is provided when the following criteria is met:

A. Member has a documented inadequate response, contraindication, or intolerable adverse event to all preferred products.

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

FACTOR VIII CONCENTRATES

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

Table: Factor VIII Concentrates and Covered Uses

Brand	Generic	FDA-Approved Indication(s)	Compendial Indication(s)
Recombinant Factor VIII Concentrates			
Advate	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Afstyla	antihemophilic factor [recombinant], single chain	Hemophilia A	
Kogenate FS	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Kovaltry	antihemophilic factor [recombinant]	Hemophilia A	
Novoeight	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Nuwiq	antihemophilic factor [recombinant]	Hemophilia A	
Recombinate	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Xyntha	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Extended Half-life Recombinant Factor VIII Concentrates			
Adynovate	antihemophilic factor [recombinant], PEGylated	Hemophilia A	
Altuviiio	antihemophilic factor [recombinant], Fc-VWF-XTEN fusion protein-ehtl	Hemophilia A	
Eloctate	antihemophilic factor [recombinant], Fc fusion protein	Hemophilia A	
Jivi	antihemophilic factor [recombinant], PEGylated-aucl	Hemophilia A	
Esperoct	antihemophilic factor [recombinant], Glycopegylated-exei	Hemophilia A	
Human Plasma-Derived Factor VIII Concentrate			

Hemofil M	antihemophilic factor [human] monoclonal antibody purified	Hemophilia A	Acquired Hemophilia A
Human Plasma-Derived Factor VIII Concentrates That Contain Von Willebrand Factor			
Alphanate **Humate-P**	antihemophilic factor/von Willebrand factor complex [human]	Hemophilia A, von Willebrand Disease	Acquired Hemophilia A, Acquired von Willebrand Syndrome
Koate	antihemophilic factor [human]	Hemophilia A	Acquired Hemophilia A, von Willebrand Disease

All other indications are considered experimental/investigational and not medically necessary.

II. PRESCRIBER SPECIALTIES

Must be prescribed by or in consultation with a hematologist.

III. CRITERIA FOR INITIAL APPROVAL

A. Hemophilia A

Authorization of 12 months of Advate, Adynovate, Afstyla, Alphanate, Altuviiio, Eloctate, Esperoct, Hemofil-M, Humate-P, Koate, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, or Xyntha may be granted for treatment of hemophilia A when either of the following criteria is met:

1. Member has mild disease (see Appendix A) and has had an insufficient response to desmopressin or a documented clinical reason for not using desmopressin (see Appendix B).
2. Member has moderate or severe disease (see Appendix A).

Authorization of 12 months of Jivi may be granted for treatment of hemophilia A when BOTH of the following criteria are met:

1. Member has previously received treatment for hemophilia A with a factor VIII product.
2. Member is ≥ 12 years of age.

B. Von Willebrand Disease (VWD)

Authorization of 12 months of Alphanate, Humate-P, or Koate may be granted for treatment of VWD when any of the following criteria is met:

1. Member has type 1, 2A, 2M, or 2N VWD and has had an insufficient response to desmopressin or a documented clinical reason for not using desmopressin (see Appendix B).
2. Member has type 2B or type 3 VWD.

C. Acquired Hemophilia A

Authorization of 12 months of Advate, Alphanate, Hemofil M, Humate-P, Koate, Kogenate FS, Novoeight, Recombinate, or Xyntha may be granted for treatment of acquired hemophilia A.

D. Acquired von Willebrand Syndrome

Authorization of 12 months of Alphanate or Humate-P may be granted for treatment of acquired von Willebrand syndrome.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an

indication listed in Section III when the member is experiencing benefit from therapy (e.g., reduced frequency or severity of bleeds).

V. APPENDICES

Appendix A: Classification of Hemophilia by Clotting Factor Level (% Activity) and Bleeding Episodes

Severity	Clotting Factor Level % activity*	Bleeding Episodes
Severe	<1%	Spontaneous bleeding episodes, predominantly into joints and muscles Severe bleeding with trauma, injury or surgery
Moderate	1% to 5%	Occasional spontaneous bleeding episodes Severe bleeding with trauma, injury or surgery
Mild	6% to 40%	Severe bleeding with serious injury, trauma or surgery

*Factor assay levels are required to determine the diagnosis and are of value in monitoring treatment response.

Appendix B: Clinical Reasons For Not Utilizing Desmopressin in Patients with Hemophilia A and Type 1, 2A, 2M and 2N VWD

A. Age < 2 years
B. Pregnancy
C. Fluid/electrolyte imbalance
D. High risk for cardiovascular or cerebrovascular disease (especially the elderly)
E. Predisposition to thrombus formation
F. Trauma requiring surgery
G. Life-threatening bleed
H. Contraindication or intolerance to desmopressin
I. Severe type 1 von Willebrand disease
J. Stimate Nasal Spray is unavailable due to backorder/shortage issues (where applicable)

REFERENCES:

SECTION 1

1. Advate [package insert]. Lexington, MA: Baxalta US Inc.; March 2023.
2. Adynovate [package insert].Takeda Pharmaceuticals U.S.A., Inc.; August 2023.
3. Afstyla [package insert]. Kankakee, IL: CSL Behring LLC; June 2023.
4. Altuviio [package insert]. Waltham, MA: Bioverativ Therapeutics Inc.; May 2024.
5. Eloctate [package insert]. Waltham, MA: Sanofi Company; May 2023.
6. Esperoct [package insert]. Plainsboro, NJ; Novo Nordisk; February 2024.
7. Jivi [package insert]. Whippany, NJ: Bayer HealthCare LLC; August 2018.
8. Hemlibra [package insert]. South San Francisco, CA: Genentech, Inc; January 2024.
9. Kogenate FS [package insert]. Whippany, NJ: Bayer HealthCare LLC; December 2019.
10. Kogenate FS with BIO-SET [package insert]. Whippany, NJ: Bayer HealthCare LLC; December 2019.
11. Kogenate FS with Vial Adapter [package insert]. Whippany, NJ: Bayer HealthCare LLC; December 2019.
12. Kovaltry [package insert]. Whippany, NJ: Bayer Healthcare LLC; December 2022.
13. Novoeight [package insert]. Plainsboro, NJ: Novo Nordisk Inc; July 2020.
14. Nuwiq [package insert]. Paramus, NJ: Octapharma USA, Inc., June 2021.
15. Recombinate [package insert]. Lexington, MA: Baxalta US Inc.; March 2023.
16. Roctavian [package insert]. Novato, CA: BioMarin Pharmaceutical Inc.; June 2023
17. Xyntha [package insert]. Philadelphia, PA; Wyeth Pharmaceuticals LLC; July 2022.

SECTION 2

1. Advate [package insert]. Lexington, MA: Takeda Pharmaceuticals U.S.A., Inc.; March 2023.
2. Jivi [package insert]. Whippany, NJ: Bayer HealthCare LLC; August 2018.

3. Kogenate FS [package insert]. Whippany, NJ: Bayer HealthCare LLC; May 2016.
4. Kogenate FS with BIO-SET [package insert]. Whippany, NJ: Bayer HealthCare LLC; May 2016.
5. Kogenate FS with Vial Adapter [package insert]. Whippany, NJ: Bayer HealthCare LLC; December 2019.
6. Kovaltry [package insert]. Whippany, NJ: Bayer Healthcare LLC; December 2022.
7. Novoeight [package insert]. Plainsboro, NJ: Novo Nordisk Inc., July 2020.
8. Nuwiq [package insert]. Paramus, NJ: Octapharma USA, Inc., June 2021.
9. Recombinate with 5 mL Sterile Water for Injection using BAXAJECT II [package insert]. Lexington, MA: Takeda Pharmaceuticals U.S.A., Inc.; March 2023.
10. Xyntha [package insert]. Philadelphia, PA: Wyeth Pharmaceuticals LLC; July 2022.
11. Xyntha Solufuse [package insert]. Philadelphia, PA: Wyeth Pharmaceuticals LLC; July 2022.
12. Adynovate [package insert]. Lexington, MA: Takeda Pharmaceuticals U.S.A., Inc.; August 2023.
13. Afstyla [package insert]. Kankakee, IL: CSL Behring LLC.; June 2023.
14. Eloctate [package insert]. Waltham, MA: Bioverativ Therapeutics Inc.; May 2023.
15. Hemofil M [package insert]. Lexington, MA: Takeda Pharmaceuticals U.S.A., Inc.; March 2023.
16. Alphanate [package insert]. Los Angeles, CA: Grifols Biologicals LLC; November 2022.
17. Humate-P [package insert]. Kankakee, IL: CSL Behring LLC; June 2020.
18. Koate [package insert]. Research Triangle Park, NC: Grifols Therapeutics LLC; June 2018.
19. Koate-DVI [package insert]. Research Triangle Park, NC: Grifols Therapeutics LLC; August 2012.
20. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed December 6, 2023.
21. National Institutes of Health. The diagnosis, evaluation, and management of von Willebrand disease. Bethesda, MD: US Dept of Health and Human Services, National Institutes of Health; 2007. NIH publication No. 08-5832.
22. Tiede A, Rand J, Budde U, et al. How I treat the acquired von Willebrand syndrome. *Blood*. 2011;117(25):6777-85.
23. Federici A, Budde U, Castaman G, Rand J, Tiede A. Current diagnostic and therapeutic approaches to patients with acquired von Willebrand syndrome: a 2013 update. *Semin Thromb Hemost*. 2013;39(2):191-201.
24. Srivastava A, Santagostino E, Dougall A, et al. WFH Guidelines for the Management of Hemophilia, 3rd edition. *Haemophilia*. 2020;26 Suppl 6:1-158. doi:10.1111/hae.14046.
25. National Hemophilia Foundation. MASAC Recommendations Concerning Products Licensed for the Treatment of Hemophilia and Selected Disorders of the Coagulation System. Revised August 2023. MASAC Document #280. https://www.hemophilia.org/sites/default/files/document/files/MASAC-Products-Licensed.pdf. Accessed December 6, 2023.
26. National Hemophilia Foundation. MASAC recommendations regarding the treatment of von Willebrand disease. Revised February 2021. MASAC Document #266. https://www.hemophilia.org/sites/default/files/document/files/266.pdf. Accessed December 6, 2023.
27. Acquired hemophilia. World Federation of Hemophilia. http://www1.wfh.org/publications/files/pdf-1186.pdf. Accessed December 6, 2023.
28. Tiede A, Collins P, Knoebl P, et al. International recommendations on the diagnosis and treatment of acquired hemophilia A. *Haematologica.* 2020;105(7):1791-1801. doi:10.3324/haematol.2019.230771.
29. Franchini M, Mannucci PM. Acquired haemophilia A: a 2013 update. *Thromb Haemost*. 2013;110(6):1114-20.
30. National Hemophilia Foundation. Hemophilia A (Factor VIII Deficiency). Available at: http://www.hemophilia.org/NHFWeb/MainPgs/MainNHF.aspx?menuid=180&contentid=45&rptname=bleeding. Accessed December 6, 2023.
31. Stimate [package insert]. King of Prussia, PA: CSL Behring LLC; June 2021.
32. Leissinger C, Carcao M, Gill JC, et al. Desmopressin (DDAVP) in the management of patients with congenital bleeding disorders. *Haemophilia*. 2014;20:158-167.
33. Reding MT, NG HJ, Poulsen LH, et al. Safety and efficacy of BAY 94-9027, a prolonged-half-life factor VIII. *Journal of thrombosis and Haemostasis*. 2017; 15: 411-9.
34. Esperoct [package insert]. Plainsboro, NJ: Novo Nordisk Inc.; August 2022.
35. Altuviiio [package insert]. Waltham, MA: Bioverativ Therapeutics Inc.; March 2023.