



Reference number
4932-A

## Aetna Medicare Part B Drug Criteria

### Factor VIII Concentrates

This policy is for Aetna Medicare members. [Find the Aetna Commercial Medical Drug Criteria.](#)

For Aetna Medicare members, National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs) will be applied to Part B drug requests when applicable. Aetna Medicare Part B Drug Criteria documents will be used in the absence of an NCD and LCD.

## POLICY

### Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Advate	antihemophilic factor [recombinant]
Adynovate	antihemophilic factor [recombinant], PEGylated
Alphanate	antihemophilic factor/von Willebrand factor complex [human]
Altuviiio	antihemophilic factor [recombinant], Fc-VWF-XTEN fusion protein-ehtl
Afstyla	antihemophilic factor [recombinant], single chain
Eloctate	antihemophilic factor [recombinant], Fc fusion protein
Esperoct	antihemophilic factor [recombinant], Glycopegylated-exei
Hemofil M	antihemophilic factor [human] monoclonal antibody purified
Humate-P	antihemophilic factor/von Willebrand factor complex [human]
Jivi	antihemophilic factor [recombinant], PEGylated-aucl
Koate	antihemophilic factor [human]

<b>Brand Name</b>	<b>Generic Name</b>
Kogenate FS	antihemophilic factor [recombinant]
Kovaltry	antihemophilic factor [recombinant]
Novoeight	antihemophilic factor [recombinant]
Nuwiq	antihemophilic factor [recombinant]
Recombinate	antihemophilic factor [recombinant]
Xyntha	antihemophilic factor [recombinant]

## 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.

All other indications will be assessed on an individual basis. Submissions for indications other than those listed in this criteria should be accompanied by supporting evidence from Medicare approved compendia.

**Table: Factor VIII Concentrates and Covered Uses<sup>1-19,20-24,34,35</sup>**

### Recombinant Factor VIII Concentrates

<b>Brand</b>	<b>Generic</b>	<b>FDA-Approved Indication(s)</b>	<b>Compendial Indication(s)</b>
Advate	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Afstyla	antihemophilic factor [recombinant], single chain	Hemophilia A	None
Kogenate FS	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Kovaltry	antihemophilic factor [recombinant]	Hemophilia A	None
Novoeight	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Nuwiq	antihemophilic factor [recombinant]	Hemophilia A	None
Recombinate	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A



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Brand	Generic	FDA-Approved Indication(s)	Compendial Indication(s)
Xyntha	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A

#### Extended Half-life Recombinant Factor VIII Concentrates

Brand	Generic	FDA-Approved Indication(s)	Compendial Indication(s)
Adynovate	antihemophilic factor [recombinant], PEGylated	Hemophilia A	None
Altuviio	antihemophilic factor [recombinant], Fc-VWF-XTEN fusion protein-ehtl	Hemophilia A	None
Eloctate	antihemophilic factor [recombinant], Fc fusion protein	Hemophilia A	None
Jivi	antihemophilic factor [recombinant], PEGylated-aucl	Hemophilia A	None
Esperoct	antihemophilic factor [recombinant], Glycopegylated-exei	Hemophilia A	None

#### Human Plasma-Derived Factor VIII Concentrate

Brand	Generic	FDA-Approved Indication(s)	Compendial Indication(s)
Hemofil M	antihemophilic factor [human] monoclonal antibody purified	Hemophilia A	Acquired Hemophilia A

## Human Plasma-Derived Factor VIII Concentrates That Contain Von Willebrand Factor

<b>Brand</b>	<b>Generic</b>	<b>FDA-Approved Indication(s)</b>	<b>Compendial Indication(s)</b>
Alphanate	antihemophilic factor/von Willebrand factor complex [human]	Hemophilia A, von Willebrand Disease	Acquired Hemophilia A, Acquired von Willebrand Syndrome
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

### Coverage Criteria

#### Hemophilia A<sup>1-19,24,25,32,34,35</sup>

Authorization of 12 months of Advate, Adynovate, Afstyla, Alphanate, Altuviio, 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:

- 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).
- 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:

- Member has previously received treatment for hemophilia A with a factor VIII product.
- Member is  $\geq 7$  years of age.

#### Von Willebrand Disease (VWD)<sup>20,21,23,24</sup>

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:

- 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).
- Member has type 2B or type 3 VWD.

#### Acquired Hemophilia A<sup>20,27-29</sup>

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.

## Acquired von Willebrand Syndrome<sup>21-23</sup>

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

### Continuation of Therapy

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Authorization for 12 months may be granted when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication.
- The requested medication is being used to treat an indication listed in the coverage criteria section.
- The member is receiving benefit from therapy (e.g., reduced frequency or severity of bleeds).

### Appendix

#### Appendix A: Classification of Hemophilia by Clotting Factor Level (% Activity) and Bleeding Episodes<sup>24,30</sup>

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

<b>Severity</b>	<b>Clotting Factor Level % activity</b>	<b>Bleeding Episodes</b>
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

#### Appendix B: Clinical Reasons For Not Utilizing Desmopressin in Patients with Hemophilia A and Type 1, 2A, 2M and 2N VWD<sup>20,25,31,32</sup>

- Age < 2 years
- Pregnancy
- Fluid/electrolyte imbalance
- High risk for cardiovascular or cerebrovascular disease (especially the elderly)
- Predisposition to thrombus formation

- Trauma requiring surgery
- Life-threatening bleed
- Contraindication or intolerance to desmopressin
- Severe type 1 von Willebrand disease
- Stimite Nasal Spray is unavailable due to backorder/shortage issues (where applicable)

## Summary of Evidence

The contents of this policy were created after examining the following resources:

- The prescribing information for the factor VIII agents listed in products referenced by this document section.
- The available compendium
  - National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
  - Micromedex DrugDex
  - American Hospital Formulary Service- Drug Information (AHFS-DI)
  - Lexi-Drugs
  - Clinical Pharmacology
- The diagnosis, evaluation, and management of von Willebrand disease. Bethesda, MD: US Dept of Health and Human Services, National Institutes of Health; 2007.
- Current diagnostic and therapeutic approaches to patients with acquired von Willebrand syndrome: a 2013 update.
- WFH Guidelines for the Management of Hemophilia, 3rd edition.
- MASAC Recommendations Concerning Products Licensed for the Treatment of Hemophilia and Selected Disorders of the Coagulation System.
- MASAC recommendations regarding the treatment of von Willebrand disease.
- Acquired hemophilia. World Federation of Hemophilia.
- International recommendations on the diagnosis and treatment of acquired hemophilia A.
- Acquired haemophilia A: a 2013 update.
- National Hemophilia Foundation. Hemophilia A (Factor VIII Deficiency).
- Desmopressin (DDAVP) in the management of patients with congenital bleeding disorders.

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for the factor VIII agents listed in section I are covered in addition to the following:

- Acquired hemophilia A for Advate, Alphanate, Hemofil M, Humate-P, Koate, Kogenate FS, Novoeight, Recombinate, Xyntha
- Acquired von Willebrand syndrome for Alphanate and Humate-P
- Von Willebrand disease for Koate

## Explanation of Rationale

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for using Advate, Adynovate, Afstyla, Alphanate, Altuviiiio, Eloctate, Esperoct, Hemofil M, Humate-P, Koate, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate and Xyntha to treat mild hemophilia A can be found in the WFH Guidelines for the Management of Hemophilia. Mild disease is defined as having a clotting factor level of 6 to 40% of normal. The patient generally experiences severe bleeding with major trauma or surgery. It is rare these patients will bleed spontaneously. Desmopressin may be the treatment of choice for patients with mild hemophilia A when factor VIII can be raised to an appropriate therapeutic level because it avoids the expense and potential hazards of using clotting factor concentrates. Desmopressin is not appropriate in all situations. Patients under 2 years of age, pregnant patients, patients with electrolytes or fluid imbalance, patients at high risk for cerebrovascular disease, predisposition to thrombus formation, patients who experienced trauma severe enough to require surgery, and patients experiencing a life-threatening bleed are not ideal candidates for desmopressin therapy.

Support for using Advate, Adynovate, Afstyla, Alphanate, Altuviiiio, Eloctate, Esperoct, Hemofil M, Humate-P, Koate, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate and Xyntha to treat moderate to severe hemophilia A can be found in the WFH Guidelines for the Management of Hemophilia. Patients with moderate to severe hemophilia A should be started on prophylaxis with factor VIII or a non-factor therapy like Hemlibra to prevent a recurring life-threatening bleed. Desmopressin is not appropriate in these patients.

Support for using Alphanate, Humate-P, and Koate to treat von Willebrand syndrome can be found in the National Institutes of Health publication called the “Diagnosis, Evaluation, and Management of von Willebrand Disease”. Humate-P and Alphanate are approved by the FDA to treat von Willebrand syndrome. Koate has been used off-label for this use as well. Regarding the use of desmopressin, Type 2B and type 3 VWD does not respond consistently to desmopressin therapy and therefore desmopressin is not considered clinically useful in these patients.

Support for using Advate, Kogenate FS, Novoeight, Recombinate, and Xyntha to treat acquired hemophilia A can be found in the AHFS-DI database maintained by the American Society of Health System Pharmacists. Antihemophilic factor (recombinant) has been used in the management of bleeding episodes in some patients with acquired hemophilia A who have low levels of inhibitors. Although antihemophilic factor therapy may be effective in some patients with low levels of acquired antihemophilic factor inhibitors when given in high doses current evidence indicates that bypassing agents are substantially more effective in achieving hemostatic control and are considered the treatment of choice in patients with this condition.

Support for using Advate, Alphanate, Hemofil M, Humate-P, Koate, Kogenate FS, Novoeight, Recombinate, and Xyntha to treat acquired hemophilia A can be found in the international recommendations on the diagnosis and treatment of acquired hemophilia A (Tiede et al, 2020). Human (plasma-derived or recombinant) factor VIII is recommended if recombinant factor VIIa, activated prothrombin complex concentrate and recombinant porcine factor VIII is unavailable, and the inhibitor titer is low.

Support for using Alphanate and Humate-P to treat acquired von Willebrand syndrome can be found in the National Institutes of Health publication called the “Diagnosis, Evaluation, and Management of von Willebrand Disease”. The guideline indicates DDAVP and VWF/FVIII concentrates are first line therapy. If a patient has an inadequate response to DDAVP and VWF/FVIII concentrates, intravenous immunoglobulin given alone was effective in controlling bleeding and raising VWF:RCo activity.

## References

1. Advate [package insert]. Lexington, MA: Takeda Pharmaceuticals U.S.A., Inc.; March 2023.
2. Jivi [package insert]. Whippany, NJ: Bayer HealthCare LLC; May 2025.
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](http://online.lexi.com/lco/action/index/dataset/complete_ashp) [available with subscription]. Accessed December 9, 2024.
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 October 2024. MASAC Document #290. <https://www.hemophilia.org/sites/default/files/document/files/MASAC-Products-Licensed.pdf>. Accessed December 9, 2024.
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 9, 2024.
27. Acquired hemophilia. World Federation of Hemophilia. <http://www1.wfh.org/publications/files/pdf-1186.pdf>. Accessed December 9, 2024.
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 9, 2024.
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.; July 2024.
35. Altuviiio [package insert]. Waltham, MA: Bioverativ Therapeutics Inc.; September 2024.

**DOCUMENT HISTORY**

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See Evidence of Coverage for a complete description of plan benefits, exclusions, limitations and conditions of coverage. Plan features and availability may vary by service area.