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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	
Helixate FS	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Kogenate FS	antihemophilic factor [recombinant]	Hemophilia A	Acquired Hemophilia A
Kovaltry	antihemophilic factor [recombinant]	Hemophilia A	
Novoeight	antihemophilic factor [recombinant]	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
Prolonged Half-life Recombinant Factor VIII Concentrate			
Adynovate	antihemophilic factor [recombinant], PEGylated	Hemophilia A	
Eloctate	antihemophilic factor [recombinant], Fc fusion protein	Hemophilia A	
Jivi	antihemophilic factor [recombinant], PEGylated-aucl	Hemophilia A	
Human Plasma-Derived Factor VIII Concentrates			
Hemofil M **Monoclate-P**	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

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Koate	antihemophilic factor [human]	Hemophilia A	Acquired Hemophilia A, von Willebrand Disease

All other indications are considered experimental/investigational and are not a covered benefit.

CRITERIA FOR INITIAL APPROVAL

A. Hemophilia A

12 months authorization of Advate, Adynovate, Afstyla, Alphanate, Eloctate, Helixate FS, Hemofil M, Humate-P, Koate, Kogenate FS, Kovaltry, Monoclate-P, 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 to severe disease (see Appendix A).

12 months authorization 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

12 months authorization 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

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

D. Acquired von Willebrand Syndrome

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

II. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria. Continuation of therapy for members switching from Helixate FS to a different recombinant Factor VII concentrate, must show treatment failure or contraindication to Kogenate FS prior to switching to any other recombinant Factor VII concentrate.

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III. 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, 2N and 2M 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

IV. REFERENCES

1. Advate [package insert]. Westlake Village, CA: Baxter Healthcare Corporation; November 2016.
2. Helixate FS [package insert]. Whippany, NJ: Bayer HealthCare LLC; May 2016.
3. JIVI [package insert]. Whippany, NJ: Bayer HealthCare LLC; August 2018.
4. Kogenate FS [package insert]. Whippany, NJ: Bayer HealthCare LLC; May 2016.
5. Kogenate FS with BIO-SET [package insert]. Whippany, NJ: Bayer HealthCare LLC; May 2016.
6. Kogenate FS with Vial Adapter [package insert]. Whippany, NJ: Bayer HealthCare LLC; May 2016.
7. Kovaltry [package insert]. Whippany, NJ: Bayer Healthcare LLC; March 2016.
8. Novoeight [package insert]. Plainsboro, NJ: Novo Nordisk Inc., November 2016.
9. Nuwiq [package insert]. Hoboken, NJ: Octapharma USA, Inc., September 2015.
10. Recombinate with 5 mL Sterile Water for Injection [package insert]. Westlake Village, CA: Baxter Healthcare Corporation; December 2010.
11. Xyntha [package insert]. Philadelphia, PA: Wyeth Pharmaceuticals Inc.; October 2014.
12. Xyntha Solufuse [package insert]. Philadelphia, PA: Wyeth Pharmaceuticals Inc.; October 2014.
13. Adynovate [package insert]. Westlake Village, CA: Baxalta US Inc.; March 2017.
14. Afstyla [package insert]. Marburg, Germany: CSL Behring GmbH. September 2017.
15. Eloctate [package insert]. Cambridge, MA: Biogen Idec Inc.; January 2017.
16. Hemofil M [package insert]. Westlake Village, CA: Baxter Healthcare Corporation; April 2012.
17. Monoclate-P [package insert]. Kankakee, IL: CSL Behring LLC; February 2014.
18. Alphanate [package insert]. Los Angeles, CA: Grifols Biologicals Inc.; March 2015.
19. Humate-P [package insert]. Kankakee, IL: CSL Behring LLC; September 2016.

Reference number(s)
1937-A
1938-A
1946-A
1939-A
1945-A
2688-A

20. Koate [package insert]. Research Triangle Park, NC: Grifols Therapeutics Inc.; February 2016.
21. 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 11, 2017.
22. 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.
23. Tiede A, Rand J, Budde U, et al. How I treat the acquired von Willebrand syndrome. *Blood*. 2011;117(25):6777-85.
24. 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.
25. Srivastava A, Brewer A, Street A, et al. Guidelines for the management of hemophilia. *Haemophilia: The Official Journal Of The World Federation Of Hemophilia* [serial online]. January 2013;19(1):e1-e47. Available from: MEDLINE Complete, Ipswich, MA. Accessed December 9, 2017.
26. National Hemophilia Foundation. MASAC recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders. Revised August 2017. MASAC Document # 250. Accessed December 8, 2017.
27. National Hemophilia Foundation. MASAC recommendations regarding the treatment of von Willebrand disease. Revised November 2016. MASAC Document #244. Accessed December 8, 2017.
27. *Acquired hemophilia*. World Federation of Hemophilia. http://www1.wfh.org/publications/files/pdf-1186.pdf. Accessed December 9, 2017.
28. Huth-Kuhne A, Baudo F, Collins P, et al. International recommendations on the diagnosis and treatment of patients with acquired hemophilia A. *Haematologica*. 2009;94(4):566-75.
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 11, 2017.
31. Clinical Consult: CVS Caremark. Clinical Programs Review. Focus on Bleeding Disorder Programs; June 2014.
32. Stimate [package insert]. King of Prussia, PA: CSL Behring LLC; June 2013.
33. Leissinger C, Carcao M, Gill JC, et al. Desmopressin (DDAVP) in the management of patients with congenital bleeding disorders. *Haemophilia*. 2014;20:158-167.
34. 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.