Clinical Policy: Factor VIII (Human, Recombinant)

Reference Number: PA.CP.PHAR.215
Effective Date: 01/18
Last Review Date: 07/18

Coding Implications
Revision Log

Description
The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness® clinical policy for factor VIII (Human – Hemofil M®, Koate®, Koate-DVI®, Monoclate-P®; Recombinant - Advate®, Adynovate®, Afstyla®, Eloctate®, Helixate FS®, Kogenate FS®, Kogenate FS with Vial Adapter®, Kogenate FS with Bio-Set®, Kovaltry®, NovoEight®, Nuwiq®, Obizur®, Recombinate®, ReFacto®, Xyntha®, Xyntha® Solofuse™).

FDA Approved Indication(s)
Factor VIII products are indicated for patients with hemophilia A for the following uses:

- Control and prevention of bleeding episodes:
  - Children and adults: Advate, Adynovate, Afstyla, Eloctate, Helixate FS, Hemofil M, Koate-DVI, Kogenate FS, Kovaltry, Monoclate-P, Novoeight, Nuwiq, Recombinate, ReFacto, Xyntha
- Perioperative management:
  - Children and adults: Advate, Adynovate, Afstyla, Eloctate, Helixate FS, Hemofil M, Koate-DVI, Kogenate FS, Kovaltry, Monoclate-P, Novoeight, Nuwiq, Recombinate, ReFacto, Xyntha
- Routine prophylaxis to prevent or reduce the frequency of bleeding episodes:
  - Children and adults: Advate, Adynovate, Afstyla, Eloctate, Helixate FS, Kogenate FS, Kovaltry, Novoeight, Nuwiq, ReFacto (short-term)
- Routine prophylaxis to prevent or reduce the frequency of bleeding episodes and to reduce the risk of joint damage in children without pre-existing joint damage:
  - Children: Helixate FS, Kogenate FS
- Treatment of acquired hemophilia A:
  - Adults: Obizur

Limitation(s) of use:

- Factor VIII products are not indicated for treatment of von Willebrand disease.
- Obizur is not indicated for the treatment of congenital hemophilia A.
- Safety and efficacy of Obizur have not been established in patients with a baseline anti-porcine factor VIII inhibitor titer of > 20 BU.

Policy/Criteria
It is the policy of health plans affiliated with Pennsylvania Health and Wellness that Advate, Adynovate, Afstyla, Eloctate, Helixate FS, Hemofil M, Koate, Koate-DVI, Kogenate FS, Kogenate FS with Vial Adapter, Kogenate FS with Bio-Set, Kovaltry, Monoclate-P, NovoEight, Nuwiq, Obizur, Recombinate, ReFacto, Xyntha, Xyntha Solofuse are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Congenital Hemophilia A (must meet all):

1. Diagnosis of congenital hemophilia A;
2. Prescribed by or in consultation with a hematologist;
3. The requested product is prescribed for one of the following purposes (a, b, or c):
    a. Control and prevention of bleeding episodes (all products except Obizur);
    b. Perioperative management (all products except Obizur);
    c. Routine prophylaxis to prevent or reduce the frequency of bleeding episodes, and
        i. Request is for Advate, Adynovate, Eloctate, Helixate FS, Kogenate FS, Novoeight, Nuwiq, or ReFacto;
4. Member does not have von Willebrand disease (VWD);
5. If factor VIII coagulant activity levels are > 5%, member has failed a trial of desmopressin acetate, unless contraindicated or clinically significant adverse effects are experienced, or an appropriate formulation of desmopressin acetate is not available;
6. Dose does not exceed the FDA approved maximum recommended dose for the relevant indications

Approval duration:
3 months (bleeding episodes/surgery)
6 months (routine prophylaxis)

B. Acquired Hemophilia A (must meet all):

1. Request is for Obizur;
2. Diagnosis of acquired hemophilia A;
3. Prescribed by or in consultation with a hematologist;
4. Request is for the control and prevention of bleeding episodes;
5. Member does not have congenital hemophilia A or VWD;
6. Dose does not exceed the FDA approved maximum recommended dose for the relevant indications.

Approval duration: 3 months

C. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. Congenital Hemophilia A (must meet all)**:**

1. Currently, receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy applies (*see PA.LTSS.PHAR.01*);
2. Member is responding positively to therapy.
3. If request is for a dose increase, new dose does not exceed the FDA approved maximum recommended dose for the relevant indications.

Approval duration:
3 months (bleeding episodes/surgery)
6 months (routine prophylaxis)

B. Acquired Hemophilia A (must meet all)**:**
1. Currently, receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy applies (*see PA.LTSS.PHAR.01*);
2. Member is responding positively to therapy.
3. If request is for a dose increase, new dose does not exceed the FDA approved maximum recommended dose for the relevant indications.

Approval duration: 3 months

C. Other diagnoses/indications (1 or 2)**:**
1. Currently, receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy, or the Continuity of Care policy applies (*see PA.LTSS.PHAR.01*);.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to PA.CP.PMN.53

Background

Description/Mechanism of Action:
Factor VIII replacement, necessary for clot formation and maintenance of hemostasis, activates factor X in conjunction with activated factor IX. Activated factor X converts prothrombin to thrombin, which converts fibrinogen to fibrin, and with factor XIII forms a stable clot.

- Congenital hemophilia A: Inherited factor VIII deficiency.
- Acquired hemophilia A: Normal factor VIII genes with development of autoantibodies (inhibitors) against factor VIII. The autoantibodies neutralize circulating factor VIII and create a functional deficiency.

Formulations (from human plasma):
Solution Reconstituted, IV:
- Hemofil M: 250; 500; 1000; 1700 (units)
- Koate: 250; 500; 1000 (units) *[replacing Koate-DVI]*
- Koate-DVI: 250; 500; 1000 (units) *[phasing out]*
- Monoclate-P: 1000; 1500 (units)

Formulations (recombinant human unless otherwise noted):
Solution Reconstituted, IV:
- Advate: 250; 500; 1000; 1500; 2000; 3000; 4000 (units)
- Adynovate (pegylated/longer-lasting): 250; 500; 750; 1000; 1500; 2000 (units)
- Afstyla: 250; 500; 1000; 2000; 3000 (units)

- Eloctate (Fc fusion/longer-lasting): 250; 500; 750; 1000; 1500; 2000; 3000; 4000; 5000; 6000 (units)
- Helixate FS: 250; 500; 1000; 2000; 3000 (units)
- Kogenate FS: 250, 500, 1000, 2000, 3000 (units)
- Kogenate FS with Bio-Set: 250, 500, 1000, 2000, 3000 (units)
- Kogenate FS with Vial Adapter: 2000; 3000 (units)
- Kovaltry: 250; 500; 1000; 2000; 3000 (units)
- NovoEight: 250; 500; 1000; 1500; 2000; 3000 (units)
- Nuwiq: 250; 500; 1000; 2000 (units)
- Obizur *(recombinant porcine):* 500 (units)
- Recombinate: 220-400; 401-800; 801-1240; 1241-1800; 1801-2400 (units)
- ReFacto: 250; 500; 1000; 2000 (units)
- Xyntha: 250, 500; 100; 2000 (units)
- Xyntha Solofuse: 250; 500; 100; 2000; 3000 (units)

Acquired hemophilia A indications and approved products:

- Treatment of bleeding episodes:
  - Adults: Obizur

    Limitations of use: Safety and efficacy of Obizur has not been established in patients with baseline antiporcine factor VIII inhibitor titer greater than 20 BU. Obizur is not indicated for the treatment of congenital hemophilia A or VWD.

Appendices
Appendix A: Abbreviation Key
IV: intravenous
VWD: von Willebrand disease

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
C9137	Injection, factor VIII (antihemophilic factor, recombinant) PEGylated, 1 IU
C9138	Injection, factor VIII (antihemophilic factor, recombinant) (Nuwiq), 1 IU
J7182	Injection, factor VIII, (antihemophilic factor, recombinant), (NovoEight), per IU
J7185	Injection, factor VIII (antihemophilic factor, recombinant) (Xyntha), per IU
J7188	Injection, factor VIII (antihemophilic factor, recombinant), per IU
J7190	Factor VIII (antihemophilic factor, human) per IU

HCPCS Codes	Description
J7192	Factor VIII (antihemophilic factor, recombinant) per IU, not otherwise specified

Reviews, Revisions, and Approvals	Date	Approval Date
Dose parameters listed. Xyntha requirements added. References reviewed and updated.	02/18	

References

1. Advate Prescribing Information. Westlake Village, CA: Baxalta US, Inc.; November 2016. Available at: www.advate.com. Accessed November 27, 2017.
2. Adynovate Prescribing Information. Westlake Village, CA: Baxalta US, Inc., March 2017. Available at: www.adynovate.com. Accessed November 27, 2017.
3. Afstyla Prescribing Information. Kankakee, IL: CSL Behring LLC, October 2014. Available at: http://labeling.cslbehring.com/PI/US/Afstyla/EN/Afstyla-Prescribing-Information.pdf. Accessed November 27, 2017.
4. Eloctate Prescribing Information. Cambridge, MA: Biogen, Inc., January 2017. Available at: www.eloctate.com. Accessed November 27, 2017.
5. Helixate FS Prescribing Information. Whippany, NJ: Bayer HealthCare LLC; May 2016. Available at: http://www.helixate.com/. Accessed November 27, 2017.
6. Hemofil M Prescribing Information. Westlake Village, CA: Baxter Healthcare Corporation; March 2017. Available at: http://www.shirecontent.com/PI/PDFs/HEMOFILM_USA_ENG.pdf. Accessed November 27, 2017.
7. Koate-DVI Prescribing Information. Research Triangle Park, NC: Grifols Therapeutics, Inc.; August 2012. Available at: www.koate-dviusa.com. Accessed November 27, 2017.
8. Kogenate FS with Vial Adapter Prescribing Information. Whippany NJ: Bayer HealthCare LLC; May 2016. Available at: www.kogenatefs.com. Accessed: November 27, 2017.
9. Monoclate-P Prescribing Information. Kankakee, IL: CSL Behring, LLC; February 2014. Available at: http://labeling.cslbehring.com/PI/US/Monoclate-P/EN/Monoclate-P-Prescribing-Information.pdf. Accessed November 27, 2017.
10. NovoEight Prescribing Information. Plainsboro, NJ: Novo Nordisk, Inc.; November 2016. Available at: http://www.novoeight.com/. Accessed November 27, 2017.
11. Nuwiq Prescribing Information. Hoboken, NJ: Octapharma; July 2017. Available at: www.nuwiq.com. Accessed November 27, 2017.
12. Recombinate Prescribing Information. Westlake Village, CA: Baxalta US Inc.; November 2015. Available at: www.recombinate.com. Accessed November 27, 2017.
13. Refacto Prescribing Information. Philadelphia, PA: Wyeth Pharmaceuticals, Inc.; December 2007. Available at: www.http://labeling.pfizer.com/showlabeling.aspx?id=140. Accessed November 27, 2017.
14. Xyntha Prescribing Information. Philadelphia, PA: Wyeth Pharmaceuticals, Inc.; October 2014. Available at: www.xyntha.com. Accessed November 27, 2017.

15. Obizur Prescribing Information. Westlake Village, CA: Baxalta US, Inc.; October 2015. Available at: www.obizur.com. Accessed November 27, 2017.
16. Kovaltry Prescribing Information. Whippany, NJ: Bayer HealthCare LLC; March 2016. Available at: www.kovaltry-us.com. Accessed November 27, 2017.
17. Srivastava A, Brewer AK, Mauser-Bunschoten EP, et al. Guidelines for the management of hemophilia. *Haemophilia.* Jan 2013; 19(1): e1-47.
18. Medical and Scientific Advisory Council (MASAC) of the National Hemophilia Foundation (NHF): Database of treatment guidelines. Available at https://www.hemophilia.org/Researchers-Healthcare-Providers/Medical-and-Scientific-Advisory-Council-MASAC/MASAC-Recommendations. Accessed November 27, 2017.