Pharmacy Policy Bulletin

Title:	Hemophilia Agents
Policy #:	Rx.01.149

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:

The intent of this policy is to communicate the medical necessity criteria for Advate®, Adynovate®, Afstyla®, Alphanate®, Alphanine SD®, Alprolix®, Bebulin®, Benefix®, Coagadex®, Corifact®, Eloctate®, Feiba NF®, Helixate FS®, Hemlibra®, Hemofil M®, Humate P®, Idelvion®, Ixinity®, Jivi®, Koate DVI®, Kogenate FS®, Kovaltry®, Monoclate P®, Mononine®, Novoeight®, Novoseven RT®, Nuwiq®, Obizur®, Profilnine®, Rebinyn®, Recombinate®, Riastap®, Rixubis®, Tretten®, Vonvendi®, Wilate®, and Xyntha®/Xyntha® Solofuse™ as provided under the member's prescription drug benefit.

Description:

Hemophilia is a bleeding disorder caused by clotting factor deficiencies. Hemophilia is a rare X-linked, congenitally acquired disease that leads to a deficiency in coagulation factor, VIII (hemophilia A) or IX (hemophilia B). Hemophilia A or B occurs in approximately 1 out of 10,000 births. Hemophilia A is more common than hemophilia B, representing approximately 80-85% of hemophilia cases. The disorder is further characterized by the percentage of serum clotting factor activity as compared to the normal range:

Severe hemophilia: clotting factor levels are less than 1% of normal
Moderate hemophilia: clotting factor levels are 1-5% of normal
Mild hemophilia: clotting factors are 5-40% of normal

ɪtment of hemophilia generally involves an infusion of the deficient factors to allow for more normalized clotting response and decreased incidence of uncontrolled bleeding events. Treatment regimens are individualized based on disease severity and may include prophylactic infusions of clotting factors, on demand infusions of clotting factors, or a combination of both. Perioperative infusions are also part of the treatment regimen.

While Hemophilia A and hemophilia B are the most common types of hemophilia, 1 in every 500,000 to 2 million people have coagulation disorders caused by deficiencies in clotting factors other than

factor VIII or IX. The products listed below include those with indications to treat these rare forms of coagulation disorders.

Drug	Factor	Hemophilia A	Hemophilia B	Acquired hemophilia	von Willebrand disease	Congenital fibrinogen deficiency	Hereditary factor X deficiency	Congenital factor XIII deficiency	control of bleeding episodes, on demand	perioperative management	routine prophylaxis
Advate®	Recombinant factor VIII	X							X	X	X
Adynovate®	Recombinant factor VIII, PEGylated	X							X		X
Afstyla®	Recombinant Factor VIII	X							X	X	X
Alphanate®	Factor VIII/ von Willebrand factor complex, human	X			X (in certain circumstances)				X	X	X
Alphanine SD®	Factor IX, human		X						X	X	X
Alprolix®	Recombinant factor IX, Fc fusion protein		X						X	X	X
Bebulin®	Factor IX complex (factors IX, II, X, VII), human		X						X	X	X
Benefix®	Factor IX, recombinant		X						X	X	X

Coagadex®	Factor X, human						X		X	X	
Corifact®	Factor XIII concentrate, human							X		X	X
Eloctate®	Recombinant factor VIII, Fc fusion protein	X							X	X	X
Feiba [NF] ®	Anti-inhibitor coagulant complex	X (with inhibitors)	X (with inhibitors)						X	X	X
Helixate FS®	Recombinant factor VIII	X							X	X	X
Hemlibra®	Factor IXa/ factor X, directed antibody	X									X
Hemofil M®	Factor VIII, human	X							X	X	X
Humate P®	Factor VIII/ von Willebrand factor complex, human	X			X (in certain circumstances)				X	X	X
Idelvion®	Factor IX, recombinant albumin fusion protein		X						X	X	X
Ixinity®	Factor IX, recombinant		X						X	X	X
Jivi®	Recombinant, PEGylat	X							X	X	X

	ed, Factor VIII										
Koate DVI®	Factor VIII, human	X							X	X	X
Kogenate FS®	Recombinant factor VIII	X							X	X	X
Kovaltry®	Recombinant factor VIII	X							X	X	X
Monoclate P®	Factor VIII, human	X							X	X	X
Mononine®	Factor IX, human		X						X	X	X
Novoeight®	Recombinant factor VIII	X							X	X	X
Novoseven RT®	Recombinant factor VIIa	X	X	X					X	X	
Nuwiq®	Recombinant factor VIII	X							X	X	X
Obizur®	Recombinant factor VIII, porcine sequence			X					X		
Profilnine®	Factor IX, human		X						X		X
Rebinyn®	Recombinant Factor IX		X						X	X	
Recombinate®	Recombinant factor VIII	X							X	X	X

Riastap®	Fibrinogen concentrate, human					X			X		
Rixubis®	Factor IX, recombinant		X						X	X	X
Tretten®	Factor XIII A subunit, recombinant							X (A subunit)			X
Vonvendi®	Von Willebrand Factor Recombinant				X				X		
Wilate®	von Willebrand/ factor VIII complex, human				X				X		
Xyntha® [Solufuse]	Recombinant factor VIII	X							X	X	X

Policy:

Advate®, Adynovate®, Afstyla®, Alphanate®, Alphanine SD®, Alprolix®, Bebulin®, Benefix®, Coagadex®, Corifact®, Eloctate®, Feiba NF®, Helixate FS®, Hemlibra®, Hemofil M®, Humate P®, Idelvion®, Ixinity®, Jivi®, Koate DVI®, Kogenate FS®, Kovaltry®, Monoclate P®, Mononine®, Novoeight®, Novoseven RT®,Nuwiq®, Obizur®, Profilnine®, Rebinyn®, Recombinate®, Riastap®, Rixubis®, Tretten®, Vonvendi®, Wilate®, Xyntha®/Xyntha® Solofuse are approved when BOTH of the following are met:

1. Diagnosis of an FDA approved indication; and
2. Prescriber is a hematologist

Black Box Warning:

Feiba® NF

Thrombotic/Thromboembolic events: Thrombotic and thromboembolic events have been reported during postmarketing surveillance following infusion of anti-inhibitor coagulant complex, particularly following the administration of high doses and/or in patients with thrombotic risk factors. Monitor patients receiving anti-inhibitor coagulant complex for signs and symptoms of thromboembolic events.

Hemlibra®

Thrombotic microangiopathy/thrombotic events: Thrombotic events have been reported when high doses of activated prothrombin complex concentrate (aPCC) was administered for 24 hours or more to patients receiving Hemlibra prophylaxis. Monitor patients for thrombotic events if aPCC is administered. Discontinue aPCC and suspend dosing of Hemlibra if symptoms occur.

Novoseven®
Serious arterial and venous thrombotic events following administration of Novoseven RT have been reported. Discuss the risks and explain the signs and symptoms of thrombotic and thromboembolic events to patients who will receive Novoseven RT. Monitor patients for signs and symptoms of activation of the coagulation system and for thrombosis.

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

Advate® (antihemophilic factor, human recombinant) [package insert]. Westlake Village, CA. Baxter Healthcare Corporation. November 2016. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=80fa03d2-cd4c-4155-9b57-1396c4fa42da&type=display#section-9. Accesses January 23, 2019.

Adynovate® (antihemophilic factor, recombinant, PEGylated) [package insert]. Westlake Village, CA. Baxalta US Inc. March 2017. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=33d8ecac-2bb9-44b5-8016-3bb37db38eb5&type=display. Accessed January 23, 2019.

Afstyla® (antihemophilic factor, recombinant, single chain) [package insert]. Kankakee, IL. CSL Berhing, LLC. September 2017. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=51f19873-a63f-4229-9477-5da4ecf31cde&type=display. Accessed January 23, 2019.

Alphanate® (antihemophilic factor/ von willebrand factor complex, human) [package insert]. Los Angeles, CA. Grifols Biologicals Inc. March 2017. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=5a7aea94-654c-4113-9014-c3137de0a931&type=display. Accessed January 23, 2019.

Alphanine SD® (coagulation factor IX, human) [package insert]. Los Angeles, CA. Grifols Biologicals Inc. March 2017. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=3e99052d-4442-4283-8915-c9a796c77008&type=display. Accessed January 23, 2019.

Alprolix® (coagulation factor IX, recombinant, Fc fusion protein) [package insert]. Cambridge, MA. Biogen Idec Inc. June 2018. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=1ae6e28d-7133-4c36-c949-4fdc82f210e9&type=display. Accessed January 23, 2019.

Bebulin® (factors IX complex, human) [package insert]. Westlake Village, CA. Baxter Healthcare Corporation. September 2018. Available from:

https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=b375a2fb-7bd4-486c-87f6-72237713d528&type=display. Accessed January 23, 2019.

BeneFIX® (coagulation factor IX, recombinant) [package insert]. Philadelphia, PA. Wyeth Pharmaceuticals Inc. June 2016. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=85faa5bc-cee5-4ef1-8d80-bdbcb7eba1e4&type=display. Accessed January 23, 2019.

Bolton-Maggs PHB. Rare coagulation disorders. Available from: http://www1.wfh.org/publication/files/pdf-1188.pdf. Accessed January 23, 2019.

Coagadex® (coagulation factor X, human) [package insert]. Durham, NC. Bio Products Laboratory USA, Inc. October 2015. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=ad20e6ff-98bc-47e6-aa00-7fb441edd2b0&type=display. Accessed January 23, 2019.

Corifact® (coagulation factor XIII, human) [package insert]. Kankakee, IL. CSL Behring LLC. September 2017. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=96f1b658-01b0-43a7-9aba-693271389a78&type=display. Accessed January 23, 2019.

Eloctate® (antihemophilic factor, recombinant, Fc fusion protein) [package insert]. Cambridge, MA. December 2017. Biogen, Inc. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=bec39fa0-1524-4e6b-897f-db0ef093085e&type=display. Accessed January 23, 2019.

Feiba® (antiinhibitor coagulant complex) [package insert]. Westlake Village, CA. Baxter Healthcare Corporation. October 2018. Available from: http://www.baxalta.com/assets/documents/feiba_us_pi.pdf. Accessed January 23, 2019.

Feiba NF® (antiinhibitor coagulant complex) [package insert]. Westlake Village, CA. Baxter Healthcare Corporation. October 2018. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=752604e5-4ea2-44f4-83ed-1569373f6412&type=display. Accessed January 23, 2019.

Helixate FS® (antihemophilic factor recombinant) [package insert]. Whippany, NJ. Bayer HealthCare LLC. September 2017. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=4e4bc43f-892a-4ca4-ad43-5383c276c61e&type=display. Accessed January 23, 2019.

Hemlibra® (antihemophilic factor, humanized) [package insert]. South San Francisco, CA. Genentech, Inc. October 2018. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=2483adba-fab6-4d1b-96c5-c195577ed071. Accessed January 23, 2019.

Hemofil M® (antihemophilic factor, human) [package insert]. Westlake Village, CA. Baxter Healthcare Corporation. February 2014. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=b8953ff7-3bba-4a0b-a486-f26fb81f05d9&type=display. Accessed January 23, 2019.

Humate-P® (antihemophilic factor/ von Willebrand factor complex, human) Kankakee, IL. CSL Behring LLC. September 2017. Available from:

https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=c5f4b63b-8d8b-45b3-b530-2f1c32a1b852&type=display. Accessed January 23, 2019.

Idelvion® (coagulation factor IX, recombinant, albumin fusion protein) [package insert]. Kankakee, IL. CSL Behring. May 2018. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=f74301bf-95e2-44ab-a8b6-98aa07b04683&type=display. Accessed January 23, 2019.

Ixinity® (coagulation factor IX, recombinant) [package insert]. Baltimore, MD. Cangene Corporation. April 2018. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=1cae46d1-f463-488a-9e8b-3431ef1de1e4&type=display. Accessed January 23, 2019.

Jivi® [antihemophilic factor (recombinant), PEGylated-aucl] [prescribing information]. Whippany, NJ. Bayer Healthcare LLC. August 2018. Available from: https://labeling.bayerhealthcare.com/html/products/pi/Jivi_PI.pdf. Accessed January 22, 2019.

Koate-DVI® (antihemophilic factor, human) [package insert]. Reasearch Triangle Park. NC. Grifols Therapeutics, Inc. May 2013. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=2f77d685-e382-b2e7-2414-0d3a3448688a&type=display. Accessed January 23, 2019.

Kogenate FS® (antihemophilic factor, recombinant) [package insert] Whippany, NJ. Bayer HealthCare LLC. May 2016. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=01c6292d-b670-415b-9d8e-7df92c0adc0f&type=display, Accessed January 23, 2019.

Kovaltry® (antihemophilic factor recombinant) [package insert]. Whippany, NJ. Bayer HealthCare LLC. March 2016. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=89ba5048-469c-4f08-a173-81b0c6f3004d&type=display. Accessed January 23, 2019.

Monoclate-P® (antihemophilic factor, human) [package insert]. Kankakee, IL. CSL Behring LLC. February 2014. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=d9c17023-cbff-4d95-8f44-ef842d59d938&type=display. Accessed January 23, 2019.

Mononine® (coagulation factor IX, human) [package insert]. Kankakee, IL. CSL Behring LLC. April 2016. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=16f35cdb-7a3b-481b-a25b-0a065aea2c9b&type=display. Accessed January 23, 2019.

Novoeight® (antihemophilic factor, recombinant) [package insert]. Plainsboro, NJ. Novo Nordisk, Inc, May 2018. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=0a19a631-f494-48ac-8cab-7d572bf7b03d&type=display. Accessed January 23, 2019.

Novoseven RT® (coagulation factor VIIa, recombinant) [package insert]. Plainsboro, NJ. Novo Nordisk, Inc, October 2018. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=ea65c32f-8518-4383-b621-17056c0eebc0&type=display. Accessed January 23, 2019.

Nuwiq® (antihemophilic factor, recombinant) [package insert].Hoboken, NJ. Octapharma USA, Inc. July 2017. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=d6cb51f8-3acd-412c-93ec-41a8017dff3e&type=display. Accessed January 23, 2019.

Obizur® (antihemophilic factor, recombinant, porcine sequence) [package insert]. Westlake Village, CA. Baxter Healthcare Corporation. May 2015. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=a69ccbb3-7648-4978-8c6d-7ca6b95a9b01&type=display. Accessed January 23, 2019.

Profilnine SD® (factor IX complex) [package insert]. Los Angeles, CA. Grisfols Biologicals Inc. January 2018. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=79821042-86a5-4a64-b621-76de0a0bbab2&type=display. Accessed January 23, 2019.

Rebinyn® (factor IX, recombinant) [package insert[. Plainsboro, NJ. Novo Nordisk Inc. 2017. : https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=0ea37235-35fd-410d-b8c4-40ba15fe1294 Available from: Accessed January 23, 2019.

Recombinate® (antihemophilic factor, recombinant) [package insert]. Westlake Village, CA. Baxter Healthcare Corporation. March 2017. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=2a569ec5-08d7-44ab-b649-384a496e173c&type=display. Accessed January 23, 2019.

Riastap® (fibrinogen injection) [package insert]. Kankakee, IL. CSL Behring LLC. October 2017. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=903dc8d0-39da-462c-9dac-004e0c7a26cc&type=display. Accessed January 23, 2019.

Rixubis® (coagulation factor IX, recombinant) [package insert]. Westlake Village, CA. Baxter Healthcare Corporation. May 2018. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=f5070a92-96b8-476a-a2dc-18b22d95e5e0&type=display. Accessed January 23, 2019.

Srivastava A, et al. Guidelines for the management of hemophilia. Available form: https://www1.wfh.org/publication/files/pdf-1472.pdf. Accessed January 23, 2019.

Tretten® (coagulation factor XIII a-subunit, recombinant) [package insert]. Plainsboro, NJ. Novo Nordisk, Inc, November 2016. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=8664978e-1814-4930-aca5-97a24455f6df&type=display. Accessed January 23, 2019.

Vonvendi® (von Willebrand factor, recombinant) [package insert]. Westlake Village, CA. Baxalta US, Inc. July 2018. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=53b6d198-6175-4a26-8606-dc0d2a0f12d6&type=display. Accessed January 23, 2019.

Wilate® (Factor VII/VWF) [package insert]. Hoboken, NJ. Octapharma USA, Inc. August 2010. Available from: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=d0379e0c-bb51-554e-a58b-b2afa60019d4&type=display. Accessed January 23, 2019.

Xyntha® (antihemophilic factor, recombinant) [package insert]. Philadelphia, PA. Wyeth Pharmaceuticals Inc. October 2014. Available from:

https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=52e97c7f-8240-4cd6-afd2-c452ab2f6e32&type=display. Accessed January 29, 2019

Applicable Drugs:

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Drug Names
Advate®
Adynovate®
Afstyla®
Alphanate®
Alphanine SD®
Alprolix®
Bebulin®
BeneFIX®
Coagadex®
Corifact®
Eloctate®
Feiba NF®
Helixate FS®
Hemlibra®
Hemofil M®
Humate-P®
Idelvion®
Ixinity®
Jivi®
Koate-DVI®
Kogenate FS®
Kovaltry®
Monoclate-P®
Mononine®
Novoeight®
Novoseven RT®
Nuwiq®
Obizur®
Profilnine SD®
Rebinyn®
Recombinate®
Riastap®

Rixubis®
Tretten®
Vonvendi®
Wilate®
Xyntha®

Cross References:

N/A

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