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Subject: Clotting Factors and Coagulant Blood Products

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DESCRIPTION:

Hemostasis is regulated by a series of complex procoagulant and anticoagulant actions that involve the vessel wall, platelets, and the coagulation and fibrinolytic systems. An imbalance in any direction can result in coagulation disorders and specifically in a bleeding disorder when there is a deficiency of coagulation factors. Coagulation factor deficiencies present more frequently as an acquired deficiency such as disseminated intravascular coagulation (DIC) or vitamin K deficiency; inherited deficiencies are rarer, with the most common being deficiencies of factor VIII (hemophilia A) and factor IX (hemophilia B). Treatment of both acquired and inherited deficiencies involve factor replacement using either recombinant or purified plasma-derived products.

Rarely, individuals develop neutralizing antibodies, or inhibitors, to factor VIII and IX resulting in a decreased clinical response to factor replacement. Inhibitors are measured with the Bethesda assay with titers reported in Bethesda units (BU). One BU is the amount of inhibitor needed to inactivate half of factor VIII or IX in a mixture of normal and inhibitor-containing plasma. Patients with inhibitors are classified as either low responders (<5 BU/mL) or high responders (≥5 BU/mL). Administering high and more frequent doses of factor products may effectively manage bleeding episodes in low responders, while high responders should be managed with agents that bypass the factor to which the antibody is directed.

A brief overview of covered clotting factors and coagulant blood products is provided in Table 1.

TABLE 1

Review of clotting factor and coagulant blood products

Product	Notes
Anti-inhibitor Coagulant Complex *Feiba*	• Bypassing agent derived from human plasma • Contains factors II, VIIa, IX, and X • Labeled with units of factor VIII bypassing activity • Decreases activated partial thromboplastin time (aPTT) • Manufacturer suggests use as a first-line agent if inhibitor titer is greater than 10 BU/mL and second-line agent if inhibitor titer is 5-10 BU/mL • Inadequate response to treatment may result from an abnormal platelet count or impaired platelet function
Fibrinogen concentrate *Fibryga, RiaSTAP*	• Derived from human plasma • Factor I is a substrate for thrombin, factor XIIIa, and plasmin
Factor VIIa *NovoSeven, NovoSeven RT*	• Bypassing agent generated from cloned human factor VII expressed in baby hamster kidney cells • Contains only activated factor VIIa • Short dosing interval (half-life: 3 hours)
Factor VIII Human: *Hemofil M, Monoclate-P* Recombinant: *Advate, Helixate FS, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, ReFacto, Xyntha*	• Products differ based on purity and source of factor VIII • Facilitates the activation of factor X causing the formation of thrombin and fibrin • Factor VIII potency differs by product
Factor VIII/VWF complex *Alphanate, Humate P, Koate-DVI, Octanate, Wilate*	• Derived from human plasma • Factor VIII facilitates the activation of factor X causing the formation of thrombin and fibrin • Von Willebrand factor promotes platelet aggregation and adhesion to damaged vascular endothelium • Factor VIII potency differs by product
von Willebrand factor, recombinant *Vonvendi*	• Purified recombinant von Willebrand factor (rVWF) expressed in Chinese Hamster Ovary (CHO) cells • Acts to promote hemostasis by mediating platelet adhesion to damaged vascular sub-endothelial matrix (e.g. collagen) and platelet

	aggregation, and as a carrier protein for factor VIII, protecting it from rapid proteolysis
Antihemophilic factor porcine, recombinant *Obizur*	• Derived from baby hamster kidney cell line which secrete recombinant porcine factor VIII in cell culture medium • Replaces the inhibited factor VIII needed for effective hemostasis and normalizes the aPTT over the effective dosing period. • Factor VIII activity, not aPTT, should not be used as a measure of efficacy during treatment
Antihemophilic factor (recombinant), single chain *Afstyla*	• Uses a covalent bond to form a single polypeptide-chain (one structural entity) to improve the stability of factor VIII and provide longer-lasting factor VIII activity
Antihemophilic factor Fc fusion protein, recombinant (rFVIIIFc) *Eloctate*	• Antihemophilic factor (Factor VIII) is covalently linked to the Fc domain of human immunoglobulin G1 • Binding of Fc domain delays degradation to increase circulating half-life of factor VIII
Antihemophilic factor (recombinant), glycopegylated-exei *Esperoct*	
Antihemophilic factor pegylated, recombinant *Adynovate*	• Pegylated form of recombinant antihemophilic factor (Factor VIII) • Exhibits an extended terminal half-life through pegylation of the parent molecule, which reduces binding to the physiological factor VIII clearance receptor (LRP1)
Antihemophilic factor (recombinant) pegylated-aucl *Jivi*	• Site-specifically PEGylated recombinant antihemophilic factor that temporarily replaces the missing coagulation Factor VIII • The site-specific PEGylation in the A3 domain reduces binding to the physiological Factor VIII clearance receptors resulting in an extended half-life and increased AUC
Emicizumab-kxwh *Hemlibra*	• Humanized monoclonal modified IgG4 antibody with a bispecific antibody structure binding factor IXa and factor X • Bridges factor IX and factor X to restore the function of missing factor VIII that is needed for effective hemostasis
Factor IX	• BeneFIX and RIXUBIS are produced in a Chinese hamster ovary

Human: *AlphaNine SD, Mononine* Recombinant: *BeneFIX, RIXUBIS, Ixinity*	cell line • Mononine is purified with a murine monoclonal antibody • Combines with factor VIII to activate factor X (factor X converts prothrombin to thrombin; thrombin converts fibrinogen to fibrin clot)
Factor IX complex *Bebulin, Profilnine SD*	• Derived from human plasma • Contains varying concentrations of factors II, VII, and X (in addition to factor IX)
Factor IX albumin fusion protein, recombinant *Idelvion*	• Recombinant factor IX molecule is genetically fused to recombinant albumin • Fusing to albumin prolongs the half-life of factor IX
Factor IX Fc fusion protein, recombinant *Alprolix*	• Human coagulation factor IX is covalently linked to the Fc domain of human immunoglobulin G1 • Binding of Fc domain delays degradation to increase circulating half-life of factor IX
Factor IX GlycoPEGylated, recombinant *Rebinyn*	• Recombinant factor IX molecule is conjugated to a polyethylene glycol molecule • Conjugating to polyethylene glycol prolongs the half-life of factor IX
Coagulation Factor X, human *Coagadex*	• Derived from human plasma • Factor X is an inactive zymogen, which can be activated by Factor IXa (via the intrinsic pathway) or by Factor VIIa (via the extrinsic pathway)
Factor XIII Human: *Corifact* Recombinant: *Tretten*	• Circulates in the blood and is found in platelets, macrophages, and monocytes • Promotes cross-linking of fibrin during the coagulation process, and protects the newly formed clot from fibrinolysis

POSITION STATEMENT:

Initiation and continuation of a clotting factor or coagulant blood product **meets the definition of medical necessity** when all of the following criteria are met:

1. Member has seen a board certified hematologist or hematologist-oncologist and that physician has performed a complete hematologic and musculoskeletal assessment in the past 12 months – documentation from medical record must be provided
2. Clotting factor or coagulant blood product is prescribed by a board certified hematologist or hematologist-oncologist

3. Factor replacement protocol (including dosing for both acute and prophylactic management) is provided
4. Factor replacement protocol (including dosing for both acute and prophylactic management) has been developed or evaluated by a board certified hematologist or hematologist-oncologist within the past 12 months – documentation from the medical record must be provided
5. Member meets product-specific criteria outlined in Table 2.

TABLE 2

Table 2. Criteria for use of clotting factor and coagulant blood products*

Product	Criteria
Anti-inhibitor Coagulant Complex *Feiba*	Initiation and continuation **meet the definition of medical necessity** if **ALL** criteria are met: 1. Member is diagnosed with one of the following: a. Hemophilia A with inhibitors b. Hemophilia B with inhibitors c. Acquired inhibitors to factors VIII, XI, and XII 2. Member has developed high-titer factor VIII or IX inhibitors (≥ 5 Bethesda units [BU]) 3. Indication for use is **ONE** of the following: a. Treatment of acute bleeding episode b. Prophylaxis of post-operative bleeding, including dental bleeding prophylaxis (e.g., tooth extraction) – documentation of planned procedure must be provided c. Routine prophylaxis of bleeding 4. Dose does not exceed indication specific limits: a. Treatment of acute bleeding episode: 200 units/kg/day b. Prophylaxis of post-operative bleeding: 100 units/kg x 1 dose c. Routine prophylaxis of bleeding: 85 units/kg every other day 5. Dispensed quantity does not exceed the following indication based limits: a. Treatment of acute bleeding episode: 5 doses b. Prophylaxis of post-operative bleeding: 1 dose/procedure c. Routine prophylaxis of bleeding: 15 doses/30 days Approval duration: 1 year
Factor VIIa *NovoSeven, NovoSeven*	Initiation and continuation **meet the definition of medical necessity** if **ALL** criteria are met:

RT	1. Indication for use is one of the following: a. Treatment of acute bleeding episode b. Prophylaxis of post-operative bleeding, including dental bleeding prophylaxis (e.g., tooth extraction) – documentation of planned procedure must be provided 2. Member is diagnosed with one of the following and dose does not exceed diagnosis specific limits: a. Member is diagnosed with hemophilia A with high-titer factor VIII inhibitors (≥ 5 Bethesda units [BU]) **AND** bolus dose does not exceed 120 mcg/kg/dose in adults or 150 mcg/kg/dose in children b. Member is diagnosed with hemophilia B with high-titer factor IX inhibitors (≥ 5 Bethesda units [BU]) **AND** bolus dose does not exceed 120 mcg/kg/dose in adults or 150 mcg/kg/dose in children c. Member is diagnosed with acquired hemophilia **AND** bolus dose does not exceed 90 mcg/kg/dose d. Member is diagnosed with a congenital factor VII deficiency **AND** bolus dose does not exceed 30 mcg/kg/dose e. Member is diagnosed with Glanzmann's thrombasthenia **AND** bolus dose does not exceed 90 mcg/kg/dose 3. Dispensed quantity does not exceed the following indication based limits: a. Treatment of acute bleeding episode: 5 doses b. Prophylaxis of post-operative bleeding: 1 dose/procedure Approval duration: 1 year
Factor VIII Human: *Hemofil M, Monoclate-P* Recombinant*: Advate, Helixate FS, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, ReFacto, Xyntha* Factor VIII/VWF complex *Alphanate, Humate P, Koate-DVI, Octanate*	Initiation and continuation **meet the definition of medical necessity** if **ANY** of the following are met: 1. Member is diagnosed with hemophilia A **AND** all of the following are met: a. Indication for use is **ONE** of the following: i. Treatment of acute bleeding episode ii. Prophylaxis of post-operative bleeding, including dental bleeding prophylaxis (e.g., tooth extraction) – documentation of planned procedure must be provided iii. Routine prophylaxis of bleeding **AND** member meets **ONE** of the following: 1. Endogenous factor VIII is less than or equal to 1 IU/dL (1%) 2. Endogenous factor VIII is less than or equal to 40 IU/dL (40%) **AND** member has

	documented history of 2 or more bleeds into large joints (i.e., ankles, knees, hips, elbows, shoulders) iv. Immune tolerance induction therapy **AND** all of the following are met: 1. Inhibitor titers are less than 10 Bethesda units/mL – laboratory documentation must be provided 2. Inhibitor titers will be measured every six months b. Dose does not exceed indication specific limits: i. Treatment of acute bleeding episode: 50 IU/kg/dose (100 IU/kg/dose if inhibitor titers are less than 10 Bethesda units/mL) ii. Prophylaxis of post-operative bleeding: 50 IU/kg/dose iii. Routine prophylaxis: 50 IU/kg/dose three times per week or every other day iv. Immune tolerance induction therapy: 200 IU/kg/day c. Dispensed quantity does not exceed the following indication based limits: i. Treatment of acute bleeding episode: 5 doses ii. Prophylaxis of post-operative bleeding: 1 dose/procedure iii. Routine prophylaxis of bleeding: 15 doses/30 days iv. Immune tolerance induction therapy: Refer to member specific protocol 2. Member is diagnosed with von Willebrand disease **AND** all of the following are met: a. Indication for use is **ONE** of the following (Alphanate, Humate P **ONLY**): i. Treatment of acute bleeding episode (Humate P) ii. Prophylaxis of post-operative bleeding, including dental bleeding prophylaxis (e.g., tooth extraction) – documentation of planned procedure must be provided b. **ONE** of the following: i. Use of desmopressin is known or suspected to be ineffective or contraindicated ii. Member was previously approved for requested product by another health plan – documentation of a recent (within 90 days prior to authorization request) health plan-paid claim for the requested product must be provided c. Dose does not exceed indication specific limits: (Alphanate,

	Humate P **ONLY**) i. Treatment of acute bleeding episode: 80 IU/kg/dose (Humate P) ii. Prophylaxis of post-operative bleeding: 60 IU/kg/dose (Alphanate, Humate P); 75 IU/kg/dose if age < 18 years (Alphanate) d. Dispensed quantity does not exceed the following indication based limits (Alphanate, Humate P **ONLY**): i. Treatment of acute bleeding episode: 5 doses (Humate P) ii. Prophylaxis of post-operative bleeding: 1 dose/procedure Approval duration: 1 year
Factor VIII/VWF complex *Wilate*	Initiation and continuation **meet the definition of medical necessity** if **ALL** criteria are met: 1. Member is diagnosed with von Willebrand disease 2. Indication for use is treatment of treatment of acute bleeding episode, including spontaneous bleeding or trauma induced bleeding 3. Member meets **ONE** of the following: a. Use of desmopressin is known or suspected to be ineffective or contraindicated b. Member was previously approved for requested product by another health plan – documentation of a recent (within 90 days prior to authorization request) health plan-paid claim for the requested product must be provided 4. Dose does not exceed 60 IU/kg/dose 5. Dispensed quantity does not exceed 5 doses Approval duration: 1 year
von Willebrand factor, recombinant *Vonvendi*	Initiation and continuation **meet the definition of medical necessity** if **ALL** criteria are met: 1. Member is diagnosed with von Willebrand disease 2. Indication for use is treatment of acute bleeding episode, including spontaneous bleeding or trauma induced bleeding 3. Member meets **ONE** of the following: a. Use of desmopressin is known or suspected to be ineffective or contraindicated b. Member was previously approved for requested product by another health plan – documentation of a recent (within 90

	days prior to authorization request) health plan-paid claim for the requested product must be provided 4. Member is 18 years of age and older 5. Dose does not exceed 80 IU/kg/dose 6. Dispensed quantity does not exceed 5 doses Approval duration: 1 year
Antihemophilic factor porcine, recombinant *Obizur*	Initiation and continuation **meet the definition of medical necessity** if **ALL** criteria are met: 1. Member is diagnosed with acquired hemophilia A 2. Indication for use is treatment of acute bleeding episode 3. Dose does not exceed 200 IU/kg/dose 4. Dispensed quantity does not exceed 5 doses Approval duration: 1 year
Antihemophilic factor (recombinant), single chain *Afstyla*	Initiation **meets the definition of medical necessity** for **ANY** of the following indications if **ALL** indication specific criteria are met: 1. Treatment of acute bleeding episode a. Member is diagnosed with hemophilia A b. Member does not have inhibitors to factor VIII c. Member has tried and had clinically evident bleeding (at indication-specific doses) after a two month trial of at least one of the following factor VIII products when used as part of a factor replacement protocol for acute management of bleeding: i. Human (plasma-derived) Factor VIII: Hemofil M, Monoclate-P ii. Recombinant Factor VIII: Advate, Helixate FS, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, ReFacto, Xyntha d. Dose does not exceed 50 IU/kg/dose e. Dispensed quantity does not exceed 5 doses 2. Prophylaxis of post-operative bleeding, including dental bleeding prophylaxis (e.g., tooth extraction) – documentation of planned procedure must be provided a. Member is diagnosed with hemophilia A b. Member does not have inhibitors to factor VIII c. Member has tried and had clinically evident bleeding (at indication-specific doses) after receiving at least one of the

	following factor VIII products when used as part of a factor replacement protocol for prophylaxis of post-operative bleeding: i. Human (plasma-derived) Factor VIII: Hemofil M, Monoclate-P ii. Recombinant Factor VIII: Advate, Helixate FS, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, ReFacto, Xyntha d. Dose does not exceed 50 IU/kg/dose e. Dispensed quantity does not exceed 1 dose/procedure 3. Routine prophylaxis of bleeding a. Member is diagnosed with hemophilia A b. Member does not have inhibitors to factor VIII c. Member meets **ONE** of the following: i. Endogenous factor VIII is less than or equal to 1 IU/dL (1%) ii. Endogenous factor VIII is less than or equal to 40 IU/dL (40%) **AND** member has documented history of 2 or more bleeds into large joints (i.e., ankles, knees, hips, elbows, shoulders) d. Member has tried and had clinically evident bleeding (1 or more episodes of spontaneous bleeding into a joint or into the central nervous system; or 4 or more episodes of soft tissue bleeding in an 8 week period) after a two month trial of at least one of the following factor VIII products when used as part of a factor replacement protocol for prophylactic management of bleeding: i. Human (plasma-derived) Factor VIII: Hemofil M, Monoclate-P ii. Recombinant Factor VIII: Advate, Helixate FS, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, ReFacto, Xyntha e. Member maintains a treatment log documenting any bleeds and required treatment for 12 consecutive months, including 6 months prior to starting treatment with Afstyla – a copy of the treatment log with at least 6 months of bleeds must be submitted f. Dose does not exceed 50 IU/kg/dose three times per week g. Dispensed quantity does not exceed 12 doses/30 days Approval duration: 6 months Continuation meets the definition of medical necessity if **ALL** criteria are met: 1. Member meets Florida Blue's initial criteria or was previously

	approved by another health plan 2. Indication for use is ONE of the following: a. Treatment of acute bleeding episode b. Prophylaxis of post-operative bleeding, including dental bleeding prophylaxis (e.g., tooth extraction) – documentation of planned procedure must be provided c. Routine prophylaxis of bleeding 3. Member maintains a treatment log documenting any bleeds and required treatment for 12 consecutive months – a copy of the treatment log must be submitted 4. Member demonstrates a beneficial response according to indication for use: a. Treatment of acute bleeding episode: Bleeding episode controlled with 2 or fewer injections b. Routine prophylaxis of bleeding: 75% reduction in ABR 5. Dose does not exceed indication-specific limits: a. Treatment of acute bleeding episode: 50 IU/kg/dose b. Prophylaxis of post-operative bleeding: 50 IU/kg/dose c. Routine prophylaxis of bleeding: 50 IU/kg/dose three times per week 6. Dispensed quantity does not exceed the following indication based limits: a. Treatment of acute bleeding episode: 5 doses b. Prophylaxis of post-operative bleeding: 1 dose/procedure c. Routine prophylaxis of bleeding: 12 doses/30 days Approval duration: 1 year
Antihemophilic factor pegylated, recombinant *Adynovate*	Initiation **meets the definition of medical necessity** for **ANY** of the following indications if **ALL** indication specific criteria are met: 1. Treatment of acute bleeding episode a. Member is diagnosed with hemophilia A b. Member does not have inhibitors to factor VIII c. Member has tried and had clinically evident bleeding (at indication-specific doses) after a two month trial of at least one of the following factor VIII products when used as part of a factor replacement protocol for acute management of bleeding: i. Human (plasma-derived) Factor VIII: Hemofil M, Monoclate-P ii. Recombinant Factor VIII: Advate, Helixate FS, Kogenate FS, Kovaltry, Novoeight, Nuwiq,

	Recombinate, ReFacto, Xyntha d. Dose does not exceed 50 IU/kg/dose e. Dispensed quantity does not exceed 5 doses 2. Routine prophylaxis of bleeding a. Member is diagnosed with hemophilia A b. Member does not have inhibitors to factor VIII c. Member meets **ONE** of the following: i. Endogenous factor VIII is less than or equal to 1 IU/dL (1%) ii. Endogenous factor VIII is less than or equal to 40 IU/dL (40%) **AND** member has documented history of 2 or more bleeds into large joints (i.e., ankles, knees, hips, elbows, shoulders) d. Member has tried and had clinically evident bleeding (1 or more episodes of spontaneous bleeding into a joint or into the central nervous system; or 4 or more episodes of soft tissue bleeding in an 8 week period) after a two month trial of at least one of the following factor VIII products when used as part of a factor replacement protocol for prophylactic management of bleeding: i. Human (plasma-derived) Factor VIII: Hemofil M, Monoclate-P ii. Recombinant Factor VIII: Advate, Helixate FS, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, ReFacto, Xyntha e. Member maintains a treatment log documenting any bleeds and required treatment for 12 consecutive months, including 6 months prior to starting treatment with Adynovate – a copy of the treatment log with at least 6 months of bleeds must be submitted f. Dose does not exceed 50 IU/kg/dose two times per week g. Dispensed quantity does not exceed 14 doses/30 days Approval duration: 6 months Continuation **meets the definition of medical necessity** if **ALL** criteria are met: 1. Member meets Florida Blue's initial criteria or was previously approved by another health plan 2. Indication for use is ONE of the following: a. Treatment of acute bleeding episode b. Prophylaxis of post-operative bleeding, including dental bleeding prophylaxis (e.g., tooth extraction) – documentation

	of planned procedure must be provided c. Routine prophylaxis of bleeding 3. Member maintains a treatment log documenting any bleeds and required treatment for 12 consecutive months – a copy of the treatment log must be submitted 4. Member demonstrates a beneficial response according to indication for use: a. Treatment of acute bleeding episode: Bleeding episode controlled with 2 or fewer injections b. Routine prophylaxis of bleeding: 75% reduction in ABR 5. Dose does not exceed indication-specific limits: a. Treatment of acute bleeding episode: 50 IU/kg/dose b. Routine prophylaxis of bleeding: 50 IU/kg/dose two times per week 6. Dispensed quantity does not exceed the following indication based limits: a. Treatment of acute bleeding episode: 5 doses b. Prophylaxis of post-operative bleeding: 1 dose/procedure c. Routine prophylaxis of bleeding: 14 doses/30 days Approval duration: 1 year
Antihemophilic factor (recombinant), glycopegylated-exei *Esperoct*	Initiation **meets the definition of medical necessity** for **ANY** of the following indications if **ALL** indication specific criteria are met: 1. Treatment of acute bleeding episode a. Member is diagnosed with hemophilia A b. Member does not have inhibitors to factor VIII c. Member has tried and had clinically evident bleeding (at indication-specific doses) after a two month trial of at least one of the following factor VIII products when used as part of a factor replacement protocol for acute management of bleeding: i. Human (plasma-derived) Factor VIII: Hemofil M, Monoclate-P ii. Recombinant Factor VIII: Advate, Helixate FS, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, ReFacto, Xyntha d. Dose does not exceed 50 IU/kg/dose e. Dispensed quantity does not exceed 5 doses 2. Prophylaxis of post-operative bleeding, including dental bleeding prophylaxis (e.g., tooth extraction) – documentation of planned procedure must be provided

	a. Member is diagnosed with hemophilia A b. Member does not have inhibitors to factor VIII c. Member has tried and had clinically evident bleeding (at indication-specific doses) after a two month trial of at least one of the following factor VIII products when used as part of a factor replacement protocol for acute management of bleeding: i. Human (plasma-derived) Factor VIII: Hemofil M, Monoclate-P ii. Recombinant Factor VIII: Advate, Helixate FS, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, ReFacto, Xyntha d. Dose does not exceed 50 IU/kg/dose e. Dispensed quantity does not exceed 1 dose/procedure 3. Routine prophylaxis of bleeding a. Member is diagnosed with hemophilia A b. Member does not have inhibitors to factor VIII c. Member meets **ONE** of the following: i. Endogenous factor VIII is less than or equal to 1 IU/dL (1%) ii. Endogenous factor VIII is less than or equal to 40 IU/dL (40%) **AND** member has documented history of 2 or more bleeds into large joints (i.e., ankles, knees, hips, elbows, shoulders) d. Member has tried and had clinically evident bleeding (1 or more episodes of spontaneous bleeding into a joint or into the central nervous system; or 4 or more episodes of soft tissue bleeding in an 8 week period) after a two month trial of at least one of the following factor VIII products when used as part of a factor replacement protocol for prophylactic management of bleeding: i. Human (plasma-derived) Factor VIII: Hemofil M, Monoclate-P ii. Recombinant Factor VIII: Advate, Helixate FS, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, ReFacto, Xyntha e. Member maintains a treatment log documenting any bleeds and required treatment for 12 consecutive months, including 6 months prior to starting treatment with Adynovate – a copy of the treatment log with at least 6 months of bleeds must be submitted f. Dose does not exceed 50 IU/kg/dose two times per week g. Dispensed quantity does not exceed 14 doses/30 days Approval duration: 6 months

	Continuation **meets the definition of medical necessity** if **ALL** criteria are met: 1. Member meets Florida Blue's initial criteria or was previously approved by another health plan 2. Indication for use is ONE of the following: a. Treatment of acute bleeding episode b. Prophylaxis of post-operative bleeding, including dental bleeding prophylaxis (e.g., tooth extraction) – documentation of planned procedure must be provided c. Routine prophylaxis of bleeding 3. Member maintains a treatment log documenting any bleeds and required treatment for 12 consecutive months – a copy of the treatment log must be submitted 4. Member demonstrates a beneficial response according to indication for use: a. Treatment of acute bleeding episode: Bleeding episode controlled with 2 or fewer injections b. Routine prophylaxis of bleeding: 75% reduction in ABR 5. Dose does not exceed indication-specific limits: a. Treatment of acute bleeding episode: 50 IU/kg/dose b. Routine prophylaxis of bleeding: 50 IU/kg/dose two times per week 6. Dispensed quantity does not exceed the following indication based limits: a. Treatment of acute bleeding episode: 5 doses b. Prophylaxis of post-operative bleeding: 1 dose/procedure c. Routine prophylaxis of bleeding: 14 doses/30 days Approval duration: 1 year
Antihemophilic factor (recombinant) pegylated-aucl *Jivi*	Initiation **meets the definition of medical necessity** for **ANY** of the following indications if **ALL** indication specific criteria are met: 1. Treatment of acute bleeding episode a. Member is diagnosed with hemophilia A b. Member does not have inhibitors to factor VIII c. Member has tried and had clinically evident bleeding (at indication-specific doses) after a two month trial of at least one of the following factor VIII products when used as part of a factor replacement protocol for acute management of

	bleeding: i. Human (plasma-derived) Factor VIII: Hemofil M, Monoclate-P ii. Recombinant Factor VIII: Advate, Helixate FS, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, ReFacto, Xyntha d. Dose does not exceed 50 IU/kg/dose e. Dispensed quantity does not exceed 5 doses 2. Prophylaxis of post-operative bleeding, including dental bleeding prophylaxis (e.g., tooth extraction) – documentation of planned procedure must be provided a. Member is diagnosed with hemophilia A b. Member does not have inhibitors to factor VIII c. Member has tried and had clinically evident bleeding (at indication-specific doses) after a two month trial of at least one of the following factor VIII products when used as part of a factor replacement protocol for acute management of bleeding: i. Human (plasma-derived) Factor VIII: Hemofil M, Monoclate-P ii. Recombinant Factor VIII: Advate, Helixate FS, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, ReFacto, Xyntha d. Dose does not exceed 50 IU/kg/dose e. Dispensed quantity does not exceed 1 dose/procedure 3. Routine prophylaxis of bleeding a. Member is diagnosed with hemophilia A b. Member does not have inhibitors to factor VIII c. Member meets **ONE** of the following: i. Endogenous factor VIII is less than or equal to 1 IU/dL (1%) ii. Endogenous factor VIII is less than or equal to 40 IU/dL (40%) **AND** member has documented history of 2 or more bleeds into large joints (i.e., ankles, knees, hips, elbows, shoulders) d. Member has tried and had clinically evident bleeding (1 or more episodes of spontaneous bleeding into a joint or into the central nervous system; or 4 or more episodes of soft tissue bleeding in an 8 week period) after a two month trial of at least one of the following factor VIII products when used as part of a factor replacement protocol for prophylactic management of bleeding: i. Human (plasma-derived) Factor VIII: Hemofil M, Monoclate-P ii. Recombinant Factor VIII: Advate, Helixate FS,

	Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, ReFacto, Xyntha e. Member maintains a treatment log documenting any bleeds and required treatment for 12 consecutive months, including 6 months prior to starting treatment with Jivi – a copy of the treatment log with at least 6 months of bleeds must be submitted f. Dose does not exceed either of the following: i. 60 IU/kg/dose two times per week ii. 45 to 60 IU/kg/dose every 5 days g. Dispensed quantity does not exceed 9 doses/30 days Approval duration: 6 months Continuation **meets the definition of medical necessity** if **ALL** criteria are met: 1. Member meets Florida Blue's initial criteria or was previously approved by another health plan 2. Indication for use is **ONE** of the following: a. Treatment of acute bleeding episode b. Prophylaxis of post-operative bleeding, including dental bleeding prophylaxis (e.g., tooth extraction) – documentation of planned procedure must be provided c. Routine prophylaxis of bleeding 3. Member maintains a treatment log documenting any bleeds and required treatment for 12 consecutive months – a copy of the treatment log must be submitted 4. Member demonstrates a beneficial response according to indication for use: a. Treatment of acute bleeding episode: Bleeding episode controlled with 2 or fewer injections b. Routine prophylaxis of bleeding: 75% reduction in ABR 5. Dose does not exceed indication-specific limits: a. Treatment of acute bleeding episode: 50 IU/kg/dose b. Routine prophylaxis of bleeding: 60 IU/kg/dose two times per week OR 45 to 60 IU/kg/dose every 5 days 6. Dispensed quantity does not exceed the following indication based limits: a. Treatment of acute bleeding episode: 5 doses b. Prophylaxis of post-operative bleeding: 1 dose/procedure c. Routine prophylaxis of bleeding: 9 doses/30 days

	Approval duration: 1 year
Antihemophilic factor Fc fusion protein, recombinant (rFVIIIFc) *Eloctate*	Initiation **meets the definition of medical necessity** for **ANY** of the following indications if **ALL** indication specific criteria are met: 1. Treatment of acute bleeding episode a. Member is diagnosed with hemophilia A b. Member does not have inhibitors to factor VIII c. Member has tried and had clinically evident bleeding (at indication-specific doses) after a two month trial of at least one of the following factor VIII products when used as part of a factor replacement protocol for acute management of bleeding: i. Human (plasma-derived) Factor VIII: Hemofil M, Monoclate-P ii. Recombinant Factor VIII: Advate, Helixate FS, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, ReFacto, Xyntha d. Dose does not exceed 50 IU/kg/dose e. Dispensed quantity does not exceed 5 doses 2. Prophylaxis of post-operative bleeding, including dental bleeding prophylaxis (e.g., tooth extraction) – documentation of planned procedure must be provided a. Member is diagnosed with hemophilia A b. Member does not have inhibitors to factor VIII c. Member has tried and had clinically evident bleeding (at indication-specific doses) after receiving at least one of the following factor VIII products when used as part of a factor replacement protocol for prophylaxis of post-operative bleeding: i. Human (plasma-derived) Factor VIII: Hemofil M, Monoclate-P ii. Recombinant Factor VIII: Advate, Helixate FS, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, ReFacto, Xyntha d. Dose does not exceed 60 IU/kg/dose e. Dispensed quantity does not exceed 1 dose/procedure 3. Routine prophylaxis of bleeding a. Member is diagnosed with hemophilia A b. Member does not have inhibitors to factor VIII c. Member meets **ONE** of the following: i. Endogenous factor VIII is less than or equal to 1

	IU/dL (1%) ii. Endogenous factor VIII is less than or equal to 40 IU/dL (40%) **AND** member has documented history of 2 or more bleeds into large joints (i.e., ankles, knees, hips, elbows, shoulders) d. Member has tried and had clinically evident bleeding (1 or more episodes of spontaneous bleeding into a joint or into the central nervous system; or 4 or more episodes of soft tissue bleeding in an 8 week period) after a two month trial of at least one of the following factor VIII products when used as part of a factor replacement protocol for prophylactic management of bleeding: i. Human (plasma-derived) Factor VIII: Hemofil M, Monoclate-P ii. Recombinant Factor VIII: Advate, Helixate FS, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, ReFacto, Xyntha e. Member maintains a treatment log documenting any bleeds and required treatment for 12 consecutive months, including 6 months prior to starting treatment with Eloctate – a copy of the treatment log with at least 6 months of bleeds must be submitted f. Dose does not exceed 65 IU/kg/dose every three to five days g. Dispensed quantity does not exceed 10 doses/30 days Approval duration: 6 months Continuation **meets the definition of medical necessity** if **ALL** criteria are met: 1. Member meets Florida Blue's initial criteria or was previously approved by another health plan 2. Indication for use is **ONE** of the following: a. Treatment of acute bleeding episode b. Prophylaxis of post-operative bleeding, including dental bleeding prophylaxis (e.g., tooth extraction) – documentation of planned procedure must be provided c. Routine prophylaxis of bleeding 3. Member maintains a treatment log documenting any bleeds and required treatment for 12 consecutive months – a copy of the treatment log must be submitted 4. Member demonstrates a beneficial response according to indication for use: a. Treatment of acute bleeding episode: Bleeding episode controlled with 2 or fewer injections

	b. Routine prophylaxis of bleeding: 75% reduction in ABR 5. Dose does not exceed indication-specific limits: a. Treatment of acute bleeding episode: 50 IU/kg/dose b. Routine prophylaxis of bleeding: 65 IU/kg/dose every three to five days 6. Dispensed quantity does not exceed the following indication based limits: a. Treatment of acute bleeding episode: 5 doses b. Prophylaxis of post-operative bleeding: 1 dose/procedure c. Routine prophylaxis of bleeding: 10 doses/30 days Approval duration: 1 year
Emicizumab-kxwh *Hemlibra*	Initiation **meets the definition of medical necessity** if **ALL** criteria are met: 1. Member is diagnosed with hemophilia A 2. Indication for use is routine prophylaxis of bleeding 3. Member meets ONE of the following: a. Endogenous factor VIII is less than or equal to 1 IU/dL (1%) b. Endogenous factor VIII is less than or equal to 40 IU/dL (40%) AND member has documented history of 2 or more bleeds into large joints (i.e., ankles, knees, hips, elbows, shoulders) 4. Member meets **ONE** of the following: a. Member has high-titer inhibitors to factor VIII (≥ 5 Bethesda units [BU]) **AND** use will not be in combination with immune tolerance therapy (ITT) b. Member does not have inhibitors to factor VIII **AND** has documentation of clinically evident bleeding (1 or more episodes of spontaneous bleeding into a joint or into the central nervous system; or 4 or more episodes of soft tissue bleeding in an 8 week period) after a six month trial of at least three of the following factor VIII products when used as part of a factor replacement protocol for prophylactic management of bleeding: i. Human (plasma-derived) Factor VIII: Hemofil M, Monoclate-P ii. Recombinant Factor VIII: Advate, Adynovate, Afstyla, Eloctate, Helixate FS, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, ReFacto, Xyntha c. Member was previously approved for Hemlibra by another health plan – documentation of a recent (within 90 days prior to authorization request) health plan-paid claim Hemlibra

	must be provided 5. Member maintains a treatment log documenting any bleeds and required treatment for 12 consecutive months, including 6 months prior to starting treatment with Hemlibra – a copy of the treatment log with at least 6 months of bleeds must be submitted 6. Dose does not exceed either of the following: a. Initial dose: 3 mg/kg once weekly for 4 weeks b. Maintenance dose: 1.5 mg/kg once weekly 7. Dispensed quantity does not exceed either of the following weight based limits per 28 days: a. Initial dose – applicable to first 28 days of therapy ONLY i. 15 kg or less: four 30 mg/1 mL vials (max 4 mL) ii. > 15 kg and ≤ 20 kg: four 60 mg/0.4 mL vials (max 1.6 mL) iii. > 20 kg and ≤ 35 kg: four 105 mg/0.7 mL vials (max 2.8 mL) iv. > 35 kg and ≤ 50 kg: four 150 mg/mL vials (max 4 mL) v. > 50 kg and ≤ 60 kg: twelve 60 mg/0.4 mL vials (max 4.8 mL) vi. > 60 kg and ≤ 70 kg: eight 105 mg/0.7 mL vials (max 5.6 mL) vii. > 70 kg and ≤ 80 kg: sixteen 60 mg/0.4 mL (max 6.4 mL) viii. > 80 kg and ≤ 100 kg: eight 150 mg/mL vials (max 8 mL) ix. > 100 kg and ≤ 105 kg: twelve 105 mg/0.7 mL vials (max 8.4 mL) x. > 105 kg and ≤ 120 kg: twenty-four 60 mg/0.4 mL vials (max 9.6 mL) xi. > 120 kg and ≤ 140 kg: sixteen 105/0.7 mL vials (max 11.2 mL) xii. > 140 kg and ≤ 150 kg: twelve 150 mg/mL vials (max 12 mL) xiii. > 150 kg and ≤ 160 kg: thirty-two 60 mg/0.4 mL vials (max 12.8 mL) xiv. > 160 kg and ≤ 175 kg: twenty 105 mg/0.7 mL vials (max 14 mL) xv. > 175 kg and ≤ 180 kg: thirty-six 60 mg/0.4 mL vials (max 14.4 mL) xvi. > 180 kg and ≤ 200 kg: sixteen 150 mg/mL vials (max 16 mL) b. Maintenance dose

	i. 20 kg or less: four 30 mg/1 mL vials (max 4 mL) ii. > 20 kg and ≤ 40 kg: four 60 mg/0.4 mL vials (max 1.6 mL) iii. > 40 kg and ≤ 70 kg: four 105 mg/0.7 mL vials (max 2.8 mL) iv. > 70 kg and ≤ 80 kg: eight 60 mg/0.4 mL vials (max 3.2 mL) v. > 80 kg and ≤ 100 kg: four 150 mg/1 mL vials (max 4 mL) vi. > 100 kg and ≤ 120 kg: twelve 60 mg/0.4 mL (max 4.8 mL) **OR** four 60 mg/0.4 mL vials (max 1.6 mL) **plus** four 105 mg/0.7 mL vials (max 2.8 mL) vii. > 120 kg and ≤ 140 kg: eight 105 mg/0.7 mL vials (max 5.6 mL) viii. > 140 kg and ≤ 160 kg: sixteen 60 mg/0.4 mL vials (max 6.4 mL) ix. > 160 kg and ≤ 200 kg: eight 150 mg/1 mL vials (max 8 mL) Approval duration: 6 months Continuation **meets the definition of medical necessity** if **ALL** criteria are met: 1. Member was previously approved by Florida Blue OR the member has previously met all initiation criteria 2. Member is diagnosed with hemophilia A 3. Indication for use is routine prophylaxis of bleeding 4. Member maintains a treatment log documenting any bleeds and required treatment for 12 consecutive months – a copy of the treatment log must be submitted 5. Member demonstrates a beneficial response to treatment with Hemlibra as evidenced by a reduction in number of bleeding events or stabilization of disease – documentation from the treatment log and/or medical record must be provided 6. Dose does not exceed: 1.5 mg/kg once weekly 7. Dispensed quantity does not exceed the following weight based limits per 28 days: a. 20 kg or less: four 30 mg/1 mL vials (max 4 mL) b. > 20 kg and ≤ 40 kg: four 60 mg/0.4 mL vials (max 1.6 mL) c. > 40 kg and ≤ 70 kg: four 105 mg/0.7 mL vials (max 2.8 mL) d. > 70 kg and ≤ 80 kg: eight 60 mg/0.4 mL vials (max 3.2 mL)

	e. > 80 kg and ≤ 100 kg: four 150 mg/1 mL vials (max 4 mL) f. > 100 kg and ≤ 120 kg: twelve 60 mg/0.4 mL (max 4.8 mL) **OR** four 60 mg/0.4 mL vials (max 1.6 mL) **plus** four 105 mg/0.7 mL vials (max 2.8 mL) g. > 120 kg and ≤ 140 kg: eight 105 mg/0.7 mL vials (max 5.6 mL) h. > 140 kg and ≤ 160 kg: sixteen 60 mg/0.4 mL vials (max 6.4 mL) i. > 160 kg and ≤ 200 kg: eight 150 mg/1 mL vials (max 8 mL) Approval duration: 1 year
Factor IX, human *AlphaNine SD, Mononine*	Initiation and continuation **meet the definition of medical necessity** if **ALL** criteria are met: 1. Member is diagnosed with hemophilia B 2. Indication for use is ONE of the following: a. Treatment of acute bleeding episode b. Prophylaxis of post-operative bleeding, including dental bleeding prophylaxis (e.g., tooth extraction) – documentation of planned procedure must be provided c. Routine prophylaxis of bleeding 3. Dose does not exceed indication specific limits: a. Treatment of acute bleeding episode: 120 IU/kg/dose b. Prophylaxis of post-operative bleeding: 100 IU/kg/dose c. Routine prophylaxis: 100 IU/kg/dose two or three times per week 4. Dispensed quantity does not exceed the following indication based limits: a. Treatment of acute bleeding episode: 5 doses b. Prophylaxis of post-operative bleeding: 1 dose/procedure c. Routine prophylaxis of bleeding: 12 doses/30 days Approval duration: 1 year
Factor IX, recombinant *BeneFIX, Ixinity, RIXUBIS*	Initiation and continuation **meet the definition of medical necessity** if **ALL** criteria are met: 1. Member is diagnosed with hemophilia B 2. Indication for use is **ONE** of the following: a. Treatment of acute bleeding episode b. Prophylaxis of post-operative bleeding, including dental

	bleeding prophylaxis (e.g., tooth extraction) – documentation of planned procedure must be provided c. Routine prophylaxis of bleeding **AND** member meets **ONE** of the following: i. Endogenous factor IX is less than or equal to 1 IU/dL (1%) ii. Endogenous factor IX is less than or equal to 40 IU/dL (40%) **AND** member has documented history of 2 or more bleeds into large joints (i.e., ankles, knees, hips, elbows, shoulders) 3. Dose does not exceed indication specific limits: a. Treatment of acute bleeding episode: 140 IU/kg/dose b. Prophylaxis of post-operative bleeding: 140 IU/kg/dose c. Routine prophylaxis of bleeding: 100 IU/kg/dose two or three times per week (BeneFIX, Ixfinity); 80 IU/kg/dose two times per week (RIXUBIS) 4. Dispensed quantity does not exceed the following indication based limits: a. Treatment of acute bleeding episode: 5 doses b. Prophylaxis of post-operative bleeding: 1 dose/procedure c. Routine prophylaxis of bleeding: 12 doses/30 days (BeneFIX, Ixfinity); 8 doses/30 days (RIXUBIS) Approval duration: 1 year
Factor IX complex *Bebulin, Profilnine SD*	Initiation and continuation **meet the definition of medical necessity** if **ALL** criteria are met: 1. Member is diagnosed with hemophilia B, factor II deficiency, or factor X deficiency 2. Indication for use is **ONE** of the following: a. Treatment of acute bleeding episode b. Prophylaxis of post-operative bleeding, including dental bleeding prophylaxis (e.g., tooth extraction) – documentation of planned procedure must be provided c. Routine prophylaxis of bleeding 3. Dose does not exceed 120 IU/kg/dose (Bebulin), 100 IU/kg/dose (Profilnine SD) 4. Dispensed quantity does not exceed the following indication based limits: a. Treatment of acute bleeding episode: 5 doses b. Prophylaxis of post-operative bleeding: 1 dose/procedure c. Routine prophylaxis of bleeding: 8 doses/30 days

	Approval duration: 1 year
Factor IX albumin fusion protein, recombinant *Idelvion*	Initiation **meets the definition of medical necessity** for **ANY** of the following indications if **ALL** indication specific criteria are met: 1. Treatment of acute bleeding episode a. Member is diagnosed with hemophilia B b. Member does not have inhibitors to factor IX c. Member has tried and had clinically evident bleeding (at indication-specific doses) after a two month trial of at least one of the following factor IX products when used as part of a factor replacement protocol for acute management of bleeding: i. Human (plasma-derived) Factor IX (human): AlphaNine SD, Mononine ii. Factor IX, recombinant: BeneFIX, Ixinity, RIXUBIS d. Dose does not exceed 100 IU/kg/dose e. Dispensed quantity does not exceed 5 doses 2. Prophylaxis of post-operative bleeding, including dental bleeding prophylaxis (e.g., tooth extraction) – documentation of planned procedure must be provided a. Member is diagnosed with hemophilia B b. Member does not have inhibitors to factor IX c. Member has tried and had clinically evident bleeding (at indication-specific doses) after a two month trial of at least one of the following factor IX products when used as part of a factor replacement protocol for prophylaxis of post-operative bleeding: i. Human (plasma-derived) Factor IX (human): AlphaNine SD, Mononine ii. Factor IX, recombinant: BeneFIX, Ixinity, RIXUBIS d. Dose does not exceed 100 IU/kg/dose e. Dispensed quantity does not exceed 1 dose/procedure 3. Routine prophylaxis of bleeding a. Member is diagnosed with hemophilia B b. Member does not have inhibitors to factor IX c. Member meets **ONE** of the following: i. Endogenous factor IX is less than or equal to 1 IU/dL (1%) ii. Endogenous factor IX is less than or equal to 40 IU/dL (40%) **AND** member has documented history of 2 or more bleeds into large joints (i.e., ankles,

	knees, hips, elbows, shoulders) d. Member has tried and had clinically evident bleeding (1 or more episodes of spontaneous bleeding into a joint or into the central nervous system; or 4 or more episodes of soft tissue bleeding in an 8 week period) after a two month trial of at least one of the following factor IX products when used as part of a factor replacement protocol for prophylactic management of bleeding t: i. Human (plasma-derived) Factor IX (human): AlphaNine SD, Mononine ii. Factor IX, recombinant: BeneFIX, Ixinity, RIXUBIS e. Member maintains a treatment log documenting any bleeds and required treatment for 12 consecutive months, including 6 months prior to starting treatment with Idelvion – a copy of the treatment log with at least 6 months of bleeds must be submitted f. Dose does not exceed: i. Age 12 years and older: 40 IU/kg one time per week or 75 IU/kg every 14 days ii. Age less than 12 years: 55 IU/kg every 7 days g. Dispensed quantity does not exceed 4 doses/28 days Approval duration: 6 months Continuation **meets the definition of medical necessity** if **ALL** criteria are met: 1. Member meets Florida Blue's initial criteria or was previously approved by another health plan 2. Indication for use is **ONE** of the following: a. Treatment of acute bleeding episode b. Prophylaxis of post-operative bleeding, including dental bleeding prophylaxis (e.g., tooth extraction) – documentation of planned procedure must be provided c. Routine prophylaxis of bleeding 3. Member demonstrates a beneficial response according to indication for use: a. Treatment of acute bleeding episode: Bleeding episode controlled with 2 or fewer injections b. Routine prophylaxis of bleeding: 75% reduction in ABR 4. Member maintains a treatment log documenting any bleeds and required treatment for 12 consecutive months – a copy of the treatment log must be submitted

	5. Dose does not exceed indication-specific limits: a. Treatment of acute bleeding episode: 100 IU/kg/dose b. Routine prophylaxis of bleeding: i. Age 12 years and older: 40 IU/kg one time per week or 75 IU/kg every 14 days ii. Age less than 12 years: 55 IU/kg every 7 days 6. Dispensed quantity does not exceed the following indication based limits: a. Treatment of acute bleeding episode: 5 doses b. Prophylaxis of post-operative bleeding: 1 dose/procedure c. Routine prophylaxis of bleeding: 4 doses/28 days Approval duration: 1 year
Factor IX Fc fusion protein, recombinant *Alprolix*	Initiation **meets the definition of medical necessity** for **ANY** of the following indications if **ALL** indication specific criteria are met: 1. Treatment of acute bleeding episode a. Member is diagnosed with hemophilia B b. Member does not have inhibitors to factor IX c. Member has tried and had clinically evident bleeding (at indication-specific doses) after a two month trial of at least one of the following factor IX products when used as part of a factor replacement protocol for acute management of bleeding: i. Human (plasma-derived) Factor IX (human): AlphaNine SD, Mononine ii. Factor IX, recombinant: BeneFIX, Ixinity, RIXUBIS d. Dose does not exceed 100 IU/kg/dose e. Dispensed quantity does not exceed 5 doses 2. Prophylaxis of post-operative bleeding, including dental bleeding prophylaxis (e.g., tooth extraction) – documentation of planned procedure must be provided a. Member is diagnosed with hemophilia B b. Member does not have inhibitors to factor IX c. Member has tried and had clinically evident bleeding (at indication-specific doses) after a two month trial of at least one of the following factor IX products when used as part of a factor replacement protocol for prophylaxis of post-operative bleeding: i. Human (plasma-derived) Factor IX (human): AlphaNine SD, Mononine

	ii. Factor IX, recombinant: BeneFIX, Ixinity, RIXUBIS d. Dose does not exceed 100 IU/kg/dose e. Dispensed quantity does not exceed 1 dose/procedure 3. Routine prophylaxis of bleeding a. Member is diagnosed with hemophilia B b. Member does not have inhibitors to factor IX c. Member meets **ONE** of the following: i. Endogenous factor IX is less than or equal to 1 IU/dL (1%) ii. Endogenous factor IX is less than or equal to 40 IU/dL (40%) **AND** member has documented history of 2 or more bleeds into large joints (i.e., ankles, knees, hips, elbows, shoulders) d. Member has tried and had clinically evident bleeding (1 or more episodes of spontaneous bleeding into a joint or into the central nervous system; or 4 or more episodes of soft tissue bleeding in an 8 week period) after a two month trial of at least one of the following factor IX products when used as part of a factor replacement protocol for prophylactic management of bleeding t: i. Human (plasma-derived) Factor IX (human): AlphaNine SD, Mononine ii. Factor IX, recombinant: BeneFIX, Ixinity, RIXUBIS e. Member maintains a treatment log documenting any bleeds and required treatment for 12 consecutive months, including 6 months prior to starting treatment with Alprolix – a copy of the treatment log with at least 6 months of bleeds must be submitted f. Dose does not exceed 50 IU/kg/dose one time per week or 100 IU/kg/dose every 10 days g. Dispensed quantity does not exceed 4 doses/28 days Approval duration: 6 months Continuation **meets the definition of medical necessity** if **ALL** criteria are met: 1. Member meets Florida Blue's initial criteria or was previously approved by another health plan 2. Indication for use is **ONE** of the following: a. Treatment of acute bleeding episode b. Prophylaxis of post-operative bleeding, including dental bleeding prophylaxis (e.g., tooth extraction) – documentation of planned procedure must be provided

	c. Routine prophylaxis of bleeding 3. Member maintains a treatment log documenting any bleeds and required treatment for 12 consecutive months – a copy of the treatment log must be submitted 4. Member demonstrates a beneficial response according to indication for use: a. Treatment of acute bleeding episode: Bleeding episode controlled with 2 or fewer injections b. Routine prophylaxis of bleeding: 75% reduction in ABR 5. Dose does not exceed indication-specific limits: a. Treatment of bleeding: 100 IU/kg/dose b. c. Routine prophylaxis of bleeding: 50 IU/kg/dose one time per week or 100 IU/kg/dose every 10 days 6. Dispensed quantity does not exceed the following indication based limits: a. Treatment of acute bleeding episode: 5 doses b. Prophylaxis of post-operative bleeding: 1 dose/procedure c. Routine prophylaxis of bleeding: 4 doses/28 days Approval duration: 1 year
Factor IX GlycoPEGylated, recombinant *Rebinyn*	Initiation **meets the definition of medical necessity** for **ANY** of the following indications if **ALL** indication specific criteria are met: 1. Treatment of acute bleeding episode a. Member is diagnosed with hemophilia B b. Member does not have inhibitors to factor IX c. Member has tried and had clinically evident bleeding (at indication-specific doses) after a two month trial of at least one of the following factor IX products when used as part of a factor replacement protocol for acute management of bleeding: i. Human (plasma-derived) Factor IX (human): AlphaNine SD, Mononine ii. Factor IX, recombinant: BeneFIX, Ixinity, RIXUBIS d. Dose does not exceed 80 IU/kg/dose e. Dispensed quantity does not exceed 5 doses 2. Prophylaxis of post-operative bleeding, including dental bleeding prophylaxis (e.g., tooth extraction) – documentation of planned procedure must be provided a. Member is diagnosed with hemophilia B

	b. Member does not have inhibitors to factor IX c. Member has tried and had clinically evident bleeding (1 or more episodes of spontaneous bleeding into a joint or into the central nervous system; or 4 or more episodes of soft tissue bleeding in an 8 week period) after a two month trial of at least one of the following factor IX products when used as part of a factor replacement protocol for prophylaxis of post-operative bleeding: i. Human (plasma-derived) Factor IX (human): AlphaNine SD, Mononine ii. Factor IX, recombinant: BeneFIX, Ixinity, RIXUBIS d. Member maintains a treatment log documenting any bleeds and required treatment for 12 consecutive months, including 6 months prior to starting treatment with Rebinyn – a copy of the treatment log with at least 6 months of bleeds must be submitted e. Dose does not exceed 80 IU/kg/dose f. Dispensed quantity does not exceed 1 dose/procedure Approval duration: 6 months Continuation **meets the definition of medical necessity** if **ALL** criteria are met: 1. Member meets Florida Blue's initial criteria or was previously approved by another health plan 2. Indication for use is ONE of the following: a. Treatment of acute bleeding episode b. Prophylaxis of post-operative bleeding, including dental bleeding prophylaxis (e.g., tooth extraction) – documentation of planned procedure must be provided 3. Member maintains a treatment log documenting any bleeds and required treatment for 12 consecutive months – a copy of the treatment log must be submitted 4. Member demonstrates a beneficial response according to indication for use: a. Treatment of bleeding: Bleeding episode controlled with 2 or fewer injections 5. Dose does not exceed indication-specific limits: a. Treatment of bleeding: 80 IU/kg/dose b. Prophylaxis of post-operative bleeding: 80 IU/kg/dose 6. Dispensed quantity does not exceed the following indication based limits:

	a. Treatment of acute bleeding episode: 5 doses b. Prophylaxis of post-operative bleeding: 1 dose/procedure Approval duration: 1 year
Fibrinogen concentrate *Fibryga, RiaSTAP*	Initiation and continuation **meet the definition of medical necessity** if **ALL** criteria are met: 1. Member is diagnosed with a congenital fibrinogen deficiency (e.g., afibrinogenemia, hypofibrinogenemia) that has been confirmed by blood coagulation testing 2. Indication for use is treatment of acute bleeding episodes 3. Use is **NOT** for treatment of dysfibrinogenemia 4. Dose does not exceed 70 mg/kg/dose unless member's baseline fibrinogen level is known Approval duration: 1 year
Coagulation Factor X, human *Coagadex*	Initiation and continuation **meet the definition of medical necessity** if **ALL** criteria are met: 1. Member is diagnosed with hereditary factor X deficiency 2. Indication for use is one of the following: a. Treatment of bleeding b. Perioperative management of bleeding AND member has mild hereditary factor X deficiency 3. Dose does not exceed indication specific limits: a. Treatment of bleeding: 25 IU/kg/dose one time every 24 hours b. Perioperative management of bleeding: 50 IU/kg/dose Approval duration: 1 year
Factor XIII, human *Corifact*	Initiation and continuation **meet the definition of medical necessity** if **ALL** criteria are met: 1. Member is diagnosed with congenital factor XIII deficiency 2. Indication for use is prophylaxis of bleeding 3. Dose does not exceed 45 IU/kg/dose every 28 days Approval duration: 1 year
Factor XIII, recombinant *Tretten*	Initiation and continuation **meet the definition of medical necessity** if **ALL** criteria are met: 1. Member is diagnosed with congenital factor XIII deficiency

	2. Indication for use is prophylaxis of bleeding 3. Dose does not exceed 35 IU/kg/dose every 28 days Approval duration: 1 year
*****Due to variations in potency and limited vial sizes, doses may be equal to or less than 110% of the doses listed above. Does not apply to Hemlibra.	

All products listed in Table 2 are considered **experimental or investigational** for all other indications as there is insufficient clinical evidence to support use.

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USE.

Dosage and administration varies considerably with each product and is based on patient weight. A brief overview of selected products is provided in Table 3; however, it is strongly recommended that the prescriber refer to product-specific labeling for complete dosing and administration instructions.

Table 3

Dosage and administration of select clotting factor and coagulant blood products	
Product	**Dosing/Administration**
Anti-inhibitor Coagulant Complex *Feiba*	**General dosing recommendation:** 50 to 100 units/kg IV (maximum total daily dose: 200 units/kg) **Joint hemorrhage:** 50 to 100 units/kg IV every 12 hours; continue until clinical improvement achieved (e.g., pain relief, reduced swelling, joint mobilization) **Mucous membrane bleeding:** 50 to 100 units/kg IV every 6 hours; carefully monitor patient and perform repeated measurements hemoglobin/hematocrit

	Soft tissue hemorrhage (e.g., retroperitoneal bleeding): 100 units/kg IV every 12 hours **Other severe hemorrhage (e.g., CNS bleed):** 100 units/kg every 6 to 12 hours; do not exceed maximum daily dose of 200 units/kg unless bleeding severity warrants use
Fibrinogen concentrate *Fibryga, RiaSTAP*	**Baseline fibrinogen concentration NOT known:** 70 mg/kg IV (rate not to exceed 5 mL/min) **Baseline fibrinogen concentration known:** Calculate dose using known and target plasma fibrinogen level as: Dose (mg/kg) = [Target plasma fibrinogen (mg/dL) – Measured plasma fibrinogen (mg/dL)] / 1.7 mg/dL **Pediatric (age less than 16 years) :** A shorter half-life and faster clearance were observed in pediatric subjects (n=4)
Factor VIIa *NovoSeven, NovoSeven RT*	**Administer by slow IV injection over 2 to 5 minutes within 3 hours of reconstitution** **Acute bleeding episodes in hemophilia A or B with inhibitors:** 90 mcg/kg every 2 hours until hemostasis achieved, then every 3 to 6 hours to maintain hemostatic plug **Bleeding prophylaxis during surgical interventions in hemophilia A or B with inhibitors:** 90 mcg/kg immediately before the intervention, then every 2 hours for the duration of the surgery • Minor surgery: Continue dosing every 2 hours for the first 48 hours after

	surgery, then every 2 to 6 hours until healing has occurred • Major surgery: Continue dosing every 2 hours for the first 5 days after surgery, then every four hours until healing has occurred **Congenital factor VII deficiency:** 15-30 mcg/kg every 4 to 6 hours until hemostasis is achieved **Acquired hemophilia:** 70 to 90 mcg/kg every 2 to 3 hours until hemostasis is achieved
Antihemophilic factor (recombinant) pegylated-aucl *Jivi*	**General Dosing Infomration:** Expected recovery: one unit per kilogram body weight will increase the Factor VIII level by 2 international units per deciliter (IU/dL) Required dose (IU) = body weight (kg) x desired Factor VIII rise (% of normal or IU/dL) x reciprocal of expected recovery (or observed recovery, if available) Estimated Increment of Factor VIII (IU/dL or % of normal) = [Total Dose (IU)/body weight (kg)] x 2 (IU/dL per IU/kg) **On-demand Treatment and Control of Bleeding Episodes** Minor event: 10 to 20 units/kg IV every 24 to 48 hours Moderate event: 15 to 30 units/kg IV every 24 to 48 hours Major event: 30 to 50 units/kg IV every 8 to 24 hours **Perioperative Management of Bleeding** Minor surgery: 15 to 30 units/kg repeat every 24 days for up to 1 day post-surgery Major surgery: 40 to 50 units/kg every 12 to 24 hours until adequate wound healing **Routine prophylaxis**

	30–40 units/kg twice weekly Adjust dose 45-60 units/kg every 5 days based on bleeding episodes
Emicizumab-kxwh *Hemlibra*	3 mg/kg by subcutaneous injection once weekly for the first 4 weeks, followed by 1.5 mg/kg once weekly
Factor XIII Human: *Corifact*	**Initial dose:** 40 IU/kg IV (rate not to exceed 4 mL/min) every 28 days to maintain 5 to 20% trough level of factor XIII activity **Dosing adjustments**: Adjust dose ± 5 IU/kg given the most recent trough factor XIII activity. Recommended dose adjustments based on the Berichrom activity assay are given as an example below: • One trough level less than 5%: Increase dose by 5 IU/kg • Trough level 5 to 20%: No change • Two trough levels of greater than 20%: Decrease dose by 5 IU/kg • One trough level greater than 25%: Decrease dose by 5 IU/kg **Perioperative management of surgical bleeding** Individualize the dose based on the factor XIII activity level, type of surgery, and clinical response. • Time since last dose is less than 7 days: Additional dose may not be needed • Time since last dose is 7 to 21 days: Partial or full dose may be needed • Time since last dose is greater than 21 days: Full dose may be given

PRECAUTIONS:

The possibility of contamination with hepatitis and other viral or bacterial infections exists for all products derived from or purified with human blood components. The manufacturing processes are designed to reduce the risk of transmitting viral infection; however, none of the processes are completely effective.

There is also the possibility that unknown infectious agents may be present. It is recommended that all members with hemophilia receive vaccination against hepatitis A and B at birth or at diagnosis of hemophilia.

Specific precautions and warnings are highlighted in Table 4.

Table 4

Precautions and warnings of clotting factor and coagulant blood products	
Product	**Precautions/Warnings**
Anti-inhibitor Coagulant Complex *Feiba*	Use is contraindicated in individuals with acute thrombosis, embolism, or significant signs of disseminated intravascular coagulation (DIC) **(Boxed Warning)**
Fibrinogen concentrate *Fibryga, RiaSTAP*	Allergic-anaphylactic reactions and thromboembolic episodes have been reported
Factor VIIa *NovoSeven, NovoSeven RT*	Arterial and venous thrombotic and thromboembolic events are associated with use **(Boxed Warning)**
Factor VIII Human: *Hemofil M, Monoclate-P* Recombinant: *Advate, Helixate FS, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, ReFacto, Xyntha*	Use with all factor VIII products has been associated with development of inhibitors. Monoclonal antibody-purified and recombinant antihemophilic factor products contain varying amounts of animal protein and should be used with caution in patients with bovine protein hypersensitivity, hamster protein hypersensitivity, and murine protein hypersensitivity.
Factor VIII/VWF complex *Alphanate, Humate P, Koate-DVI, Octanate, Wilate*	Contraindicated in individuals with known anaphylactic or severe systemic reaction to human plasma-derived products. Use has been associated with development of factor VIII or VWF inhibitors.
von Willebrand factor, recombinant *Vonvendi*	Use has been associated with development of factor VIII or VWF inhibitors.
Antihemophilic factor porcine, recombinant *Obizur*	Contraindicated in individuals with known anaphylactic or severe systemic reaction to hamster protein.
Antihemophilic factor (recombinant), single chain *Afstyla*	Hypersensitivity reactions, including anaphylaxis, are possible. Development of Factor VIII neutralizing antibodies (inhibitors) can occur. If expected plasma Factor VIII activity levels are not attained, or if bleeding is not controlled with an appropriate dose, perform an assay that measures Factor VIII inhibitor concentration. If the one-stage clotting assay is used, multiply the result by a conversion factor of 2 to determine the patient's Factor VIII activity level
Antihemophilic Fc fusion protein, recombinant (rFVIIIFc) *Eloctate*	Allergic-anaphylactic reactions have been reported
Antihemophilic factor pegylated, recombinant *Adynovate*	Allergic-anaphylactic reactions have been reported

Antihemophilic factor (recombinant), glycopegylated-exei *Esperoct*	Allergic-anaphylactic reactions have been reported. Development of Factor VIII neutralizing antibodies can occur.
Antihemophilic factor (recombinant) pegylated-aucl *Jivi*	Contraindicated in patients who have a history of hypersensitivity reactions to the active substance, polyethylene glycol (PEG), mouse or hamster proteins, or other constituents of the product. Development of Factor VIII neutralizing antibodies can occur.
Emicizumab-kxwh *Hemlibra*	Cases of thrombotic microangiopathy and thrombotic events were reported when on average a cumulative amount of >100 U/kg/24 hours of activated prothrombin complex concentrate was administered for 24 hours or more to patients receiving Hemlibra prophylaxis. Monitor for the development of thrombotic microangiopathy and thrombotic events if aPCC is administered. Discontinue aPCC and suspend dosing if symptoms occur.
Factor IX Human: *AlphaNine SD, Mononine* Recombinant: *BeneFIX, RIXUBIS, Ixinity*	BeneFIX and RIXUBIS are contraindicated in individuals with a known history of hamster protein hypersensitivity. Mononine should not be used in those with murine protein hypersensitivity. Use of all factor IX products have been associated with development of factor IX inhibitors.
Factor IX albumin fusion protein, recombinant *Idelvion*	Contraindicated in individuals with known anaphylactic or severe systemic reaction to hamster protein.
Factor IX Fc fusion protein, recombinant *Alprolix*	Allergic-anaphylactic reactions and thromboembolic episodes have been reported
Factor IX complex *Bebulin, Profilnine SD*	Individuals who receive infusions of blood or plasma products may develop signs and/or symptoms of some viral infections
Factor IX GlycoPEGylated, recombinant *Rebinyn*	Allergic-anaphylactic reactions and thromboembolic episodes have been reported
Coagulation Factor X, human *Coagadex*	Hypersensitivity reactions, including anaphylaxis, are possible. Development of neutralizing antibodies (inhibitors) may occur.
Factor XIII Human: *Corifact*	Contraindicated in individuals with known anaphylactic or severe systemic reaction to human plasma-derived products. Use has been associated with development of factor XIII inhibitors.

BILLING/CODING INFORMATION:

The following codes may be used to report clotting factor and coagulant blood products:

HCPCS Coding:

J7170	Injection, emicizumab-kxwh, 0.5 mg
J7175	Injection, factor x, (human), 1 IU [for Coagadex only]

J7177	Injection, human fibrinogen concentrate, Fibryga, 1 mg
J7178	Injection, human fibrinogen concentrate, not otherwise specified1 mg
J7179	Injection, von willebrand factor (recombinant), Vonvendi, 1 IU vwf:rco
J7180	Injection, factor XIII (antihemophilic factor, human), 1 IU
J7181	Injection, factor XIII A-subunit, (recombinant), per IU
J7182	Injection, factor viii, (antihemophilic factor, recombinant), Novoeight, per IU
J7183	Injection, von Willebrand factor complex (human), Wilate®, 1 IU VWF:RCO
J7185	Injection, factor VII (antihemophilic factor, recombinant), Xyntha, per IU
J7186	Injection, antihemophilic factor VIII/Von Willebrand factor complex (human), per factor VIII IU
J7187	Injection, von Willebrand Factor complex, Humate-P, per IU vWF-RCO
J7188	Injection, factor viii (antihemophilic factor, recombinant), Obizur, per IU
J7189	Factor VIIa (antihemophilic factor, recombinant), per 1 mcg
J7190	Factor VIII (antihemophilic factor, human), per IU
J7192	Factor VIII (antihemophilic factor, recombinant), per IU, not otherwise specified
J7193	Factor IX (antihemophilic factor, purified, nonrecombinant), per IU
J7194	Factor IX complex, per IU
J7195	Factor IX (antihemophilic factor, recombinant), per IU
J7198	Anti-inhibitor, per IU
J7199	Hemophilia clotting factor, not otherwise classified
J7200	Injection, factor IX, (antihemophilic factor, recombinant), Rixubis, per IU
J7201	Injection, factor IX, Fc fusion protein (recombinant), Alprolix, 1 IU
J7202	Injection, factor ix, albumin fusion protein, (recombinant), Idelvion, 1 IU
J7203	Injection factor ix, (antihemophilic factor, recombinant), glycopegylated, (Rebinyn), 1 IU
J7205	Injection, factor viii fc fusion protein (recombinant), per IU
J7207	Injection, factor viii, (antihemophilic factor, recombinant), pegylated, 1 IU
J7208	Injection, factor viii, (antihemophilic factor, recombinant), pegylated-aucl, (jivi), 1 IU
J7209	Injection, factor viii, (antihemophilic factor, recombinant), Nuwiq, 1 IU
J7210	Injection, factor viii, (antihemophilic factor, recombinant), Afstyla, 1 IU
J7211	Injection, factor viii, (antihemophilic factor, recombinant), Kovaltry, 1 IU

ICD-10 Diagnosis Codes That Support Medical Necessity:

D66	Hereditary factor VIII deficiency
D67	Hereditary factor IX deficiency
D68.0	Von Willebrand's disease
D68.1	Hereditary factor XI deficiency
D68.2	Hereditary deficiency of other clotting factors
D68.31	Hemorrhagic disorder due to intrinsic circulating anticoagulants
D68.32	Hemorrhagic disorder due to extrinsic circulating anticoagulants

D68.4	Acquired coagulation factor deficiency
D69.1	Qualitative platelet defects

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: BCBSF has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage Products: The following National Coverage Determination (NCD) was reviewed on the last guideline revised date: Anti-Inhibitor Coagulant Complex (AICC) (110.3) located at cms.gov. The following Local Coverage Determination (LCD) located at www.fcso.com was reviewed on the last guideline revised date: Hemophilia Clotting Factors (L33684).

DEFINITIONS:

Afibrinogenemia: lack of fibrinogen (coagulation factor I) in the blood.

AHF: Nonspecific antihemophilic factor is a preparation of factor VIII administered intravenously for the prevention or treatment of hemorrhage in patients with hemophilia A and the treatment of von Willebrand disease, hypofibrinogenemia and factor VIII deficiency.

AICC: Anti-Inhibitor Coagulant Complex is a concentrated fraction from pooled human plasma, which includes various coagulation factors. It is administered intravenously as an antihemorrhagic in hemophilic patients with inhibitors to factor XIII.

Congenital Afibrinogenemia: a rare autosomal recessive hemorrhagic coagulation disorder, characterized by complete incoagulability of the blood; hemorrhagic manifestations vary from mild to serious.

Dysfibrinogenemia: the presence in the blood of abnormal fibrinogen; both autosomal dominant and recessive forms are known.

Hemophilia B (Christmas Disease): a common type of hemophilia, an X-linked condition caused by deficiency of factor IX.

Hypofibrinogenemia: abnormally low levels of fibrinogen in the blood; called also fibrinogenopenia.

RELATED GUIDELINES:

None applicable.

OTHER:

Guidelines to first and second choice treatment:

Patient's Inhibitor	Clinical Situation		
Titer	Minor bleeding	Major bleeding	Surgery (emergency)
Less than 5 BU	AHF	AHF	AHF
5 to 10 BU	AHF	AHF	AHF
	AICC	AICC	AICC
More than 10 BU	AICC	AICC	AICC

REFERENCES:

1. Bayer. JIVI (antihemophilic factor (recombinant) pegylated-aucl) lyophilized powder for solution. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=f04e5bd5-d7e2-453b-a407-2616d81a695d.
2. Baxalta. ADYNOVATE (antihemophilic factor (recombinant) pegylated) kit. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=33d8ecac-2bb9-44b5-8016-3bb37db38eb5.
3. Baxter Healthcare Corporation. ADVATE (antihemophilic factor, human recombinant) kit. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=91ca765f-fe58-4dee-a7eb-c8d3de9f115a/.
4. Baxter Healthcare Corporation. FEIBA (anti-inhibitor coagulant complex) powder for solution. 2019 [cited 3/30/19]. Available from: http://www.feiba.com/us/forms/feiba_pi.pdf/.
5. Baxter Healthcare Corporation. HEMOFIL M (antihemophilic factor human) kit. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=b8953ff7-3bba-4a0b-a486-f26fb81f05d9/.
6. Baxter Healthcare Corporation. OBIZURE (antihemophilic factor porcine, b-domain truncated recombinant) kit. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=b8953ff7-3bba-4a0b-a486-f26fb81f05d9/."
7. Baxter Healthcare Corporation. RECOMBINATE (antihemophilic factor recombinant) kit. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=2a569ec5-08d7-44ab-b649-384a496e173c/.
8. Baxter Healthcare Corporation. RIXUBIS (coagulation factor ix recombinant human) kit. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=f5070a92-96b8-476a-a2dc-18b22d95e5e0/.
9. Bayer Healthcare. KOGENATE FS (antihemophilic factor (recombinant)) kit. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=01c6292d-b670-415b-9d8e-7df92c0adc0f/.
10. Bayer Healthcare. KOVALTRY (antihemophilic factor (recombinant)) kit. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=89ba5048-469c-4f08-a173-81b0c6f3004d/.

11. Biogen Idec Inc. ALPROLIX (coagulation factor ix (recombinant), fc fusion protein) kit. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=1ae6e28d-7133-4c36-c949-4fdc82f210e9/.
12. Biogen Idec Inc. ELOCTATE (antihemophilic factor (recombinant), fc fusion protein) kit. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=bec39fa0-1524-4e6b-897f-db0ef093085e/.
13. Cangene BioPharma. IXINITY (coagulation factor ix (recombinant)) kit. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=1cae46d1-f463-488a-9e8b-3431ef1de1e4/.
14. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 20192019 [cited 3/30/19]. Available from: http://www.clinicalpharmacology.com/.
15. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine; 20192019 [cited 3/30/19]. Available from: http://clinicaltrials.gov/.
16. CSL Behring LLC. AFSTYLA (Antihemophilic Factor (Recombinant), Single Chain) injection. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=51f19873-a63f-4229-9477-5da4ecf31cde.
17. CSL Behring LLC. CORIFACT (factor xiii concentrate (human)) kit. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=96f1b658-01b0-43a7-9aba-693271389a78/.
18. CSL Behring LLC. HELIXATE FS (antihemophilic factor, recombinant) kit. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=4e4bc43f-892a-4ca4-ad43-5383c276c61e/.
19. CSL Behring LLC. HUMATE-P (antihemophilic factor/von willebrand factor complex (human)) kit. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=c5f4b63b-8d8b-45b3-b530-2f1c32a1b852/.
20. CSL Behring LLC. IDELVION (coagulation factor IX (recombinant), albumin fusion protein) kit. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=f74301bf-95e2-44ab-a8b6-98aa07b04683.
21. CSL Behring LLC. MONOCLATE-P (antihemophilic factor human) kit. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=d9c17023-cbff-4d95-8f44-ef842d59d938/.
22. CSL Behring LLC. MONONINE (coagulation factor ix human) kit. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=16f35cdb-7a3b-481b-a25b-0a065aea2c9b/.
23. CSL Behring LLC. RIASTAP (fibrinogen) injection, powder, lyophilized, for solution. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=903dc8d0-39da-462c-9dac-004e0c7a26cc/.
24. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex2019 [cited 3/30/19]. Available from: http://www.thomsonhc.com/.

25. Genentech, Inc. HEMLIBRA (emicizumab injection) solution. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=2483adba-fab6-4d1b-96c5-c195577ed071
26. Grifols USA, LLC. ALPHANATE (antihemophilic factor/von willebrand factor complex (human)) kit. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=5a7aea94-654c-4113-9014-c3137de0a931/.
27. Grifols USA, LLC. ALPHANINE SD (coagulation factor ix (human)) kit. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=3e99052d-4442-4283-8915-c9a796c77008/.
28. Kedrion Biopharma Inc. KOATE -DVI (antihemophilic factor (human)) kit. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=2f77d685-e382-b2e7-2414-0d3a3448688a/.
29. Mahlangu J1, Powell JS, Ragni MV, et al. Phase 3 study of recombinant factor VIII Fc fusion protein in severe hemophilia A. Blood. 2014 Jan 16;123(3):317-25
30. Novo Nordisk. ESPEROCT (Antihemophilic factor (recombinant), glycopegylated-exei) powder. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: https://www.fda.gov/downloads/BiologicsBloodVaccines/UCM631602.pdf/.
31. Novo Nordisk. NOVOSEVEN RT (coagulation factor viia (recombinant)) kit. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=ea65c32f-8518-4383-b621-17056c0eebc0/.
32. Novo Nordisk. REBINYN (Coagulation Factor IX (Recombinant), GlycoPEGylated) lyophilized powder for solution for intravenous injection. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available at: https://www.fda.gov/downloads/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/FractionatedPlasmaProducts/UCM561316.pdf
33. Octapharma. WILATE - VON WILLEBRAND FACTOR/COAGULATION FACTOR VIII COMPLEX (HUMAN) (von willebrand factor/coagulation factor viii complex (human)) powder, for solution. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=d0379e0c-bb51-554e-a58b-b2afa60019d4/.
34. Octapharma. Fibryga (fibrinogen concentrate). 2019 [cited 1/31/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=007a93f4-d84b-1fa9-51ed-32f6140bf423/.
35. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2019 [cited 3/30/19]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.
36. Powell JS, Pasi KJ, Ragni MV, et al. Phase 3 study of recombinant factor IX Fc fusion protein in hemophilia B. N Engl J Med. 2013 Dec 12;369(24):2313-23.
37. Powell J, Shapiro A, Ragni M, et al. Switching to recombinant factor IX Fc fusion protein prophylaxis results in fewer infusions, decreased factor IX consumption and lower bleeding rates. Br J Haematol. 2015 Jan;168(1):113-23.
38. Wyeth Pharmaceuticals Inc. BENEFIX (coagulation factor ix (recombinant)) kit. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from:

http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=85faa5bc-cee5-4ef1-8d80-bdbcb7eba1e4/.

39. Wyeth Pharmaceuticals Inc. REFACTO (antihemophilic factor (recombinant)). 2019 [cited 3/30/19]. Available from: http://www.abopharmaceuticals.com/ProductSheets/Refacto.pdf/.
40. Wyeth Pharmaceuticals Inc. XYNTHA (antihemophilic factor (recombinant, plasma/albumin-free)) kit. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=25ea1c3c-14a2-ef11-302e-012bd683924f/.
41. Novo Nordisk. TRETTEN (coagulation factor xiii a-subunit (recombinant)) kit. 2019 [cited 3/30/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=8664978e-1814-4930-aca5-97a24455f6df/
42. Srivastava A, Brewer AK, Mauser-Bunschoten EP, et al; Treatment Guidelines Working Group on Behalf of The World Federation Of Hemophilia. Guidelines for the management of hemophilia. Haemophilia. 2013 Jan;19(1):e1-47

COMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 11/13/19.

GUIDELINE UPDATE INFORMATION:

03/15/01	New Medical Coverage Guideline.
04/15/03	Reviewed with no changes.
01/01/06	Annual HCPCS coding update: added new code J7190 and revised codes J7191 – J7193.
06/15/06	Reviewed with changing of HCPCS codes that were listed as CPT-4 codes and deleted one HCPCS code that was for Factor IX. Also added brand names.
03/15/07	MCG changed to No Longer Reviewed (NLR).
07/15/07	Reviewed guideline: maintain current coverage and limitations. Reformatted guideline, updated internet links and references.
01/01/08	Annual HCPCS coding update: added HCPCS code J7187.
09/15/08	Review and revision to guideline; consisting of renaming guideline, added factor VIIa and factor IX, updated “Description” section, updated position statement, updated coding and updated references and links.
01/01/09	Annual HCPCS coding update: deleted 90765 and 90766; added J7186, 96365 and 96366.
07/01/09	HCPCS 3rd quarter coding update: added Q2023.
10/15/09	Review and revision to guideline; consisting of Incorporating Anti-Inhibitor Coagulant Complex into MCG, adding fibrinogen and updating references.
01/01/10	Annual HCPCS coding update: added J1680 and J7185, revised J7192 descriptor, and deleted Q2023.
05/15/10	Review and revision to guideline; consisting of updating drug lists, ICD-9 coding and HCPCS codes.
01/01/11	Revision to guideline; consisting of updating coding.
05/15/11	Review and revision to guideline; consisting of adding new agent, updating dosing and references.

07/01/11	Revision to guideline; consisting of updating coding.
10/01/11	Revision to guideline; consisting of updating coding.
01/01/12	Revision to guideline; consisting updating coding.
05/15/12	Review and revision to guideline; consisting of updating of descriptions, reformatting updating coding and references
01/01/13	Annual HCPCS Update; added HCPCS code J7178 and removed J1680.
05/15/13	Review and revision to guideline; consisting of updating references, reformatting position statement.
12/15/13	Revision to guideline; consisting of description, position statement, precautions/warnings, and references.
05/15/14	Review and revision to guideline; consisting of position statement, dosage/administration, references, program exceptions.
09/15/14	Revision to guideline; consisting of description, position statement, dosage/administration, precautions, coding, references
01/01/15	Revision to guideline; consisting of coding, position statement, and annual HCPCS coding update.
03/15/15	Revision to guideline; consisting of position statement, coding.
05/15/15	Revision to guideline; consisting of position statement, precautions, references.
09/15/15	Revision to guideline; consisting of position statement, precautions, references.
10/01/15	Revision consisting of update to Program Exceptions section.
01/01/16	Annual HCPCS coding update: added codes J7188 and J7205 and delete code Q9975.
02/15/16	Revision to guideline; consisting of updating position statement.
03/15/16	Revision to guideline; consisting of updating position statement with new FDA approved agents, change MCG name from Antihemophilic Agents to Clotting Factor and Coagulant Blood Products.
04/01/16	Revision to guideline consisting of adding codes C9137 and C9138.
05/15/16	Review and revision to guideline consisting of updating position statement with newly approved agents, updating coding, references.
06/15/16	Revision to guidline consisting of updating coding.
07/15/16	Revision to guideline consisting of updating position statement.
09/15/16	Revision to guideline consisting of updating position statement to include Afstyla.
10/01/16	Revision: New HCPCS code C9139 added.
01/01/17	Revision: added HCPCS codes J7175, J7179, J7202, J7207, and J7209.
05/15/17	Review and revision to guidelines; consisting of updating references.
01/01/18	Updated HCPCS coding
01/15/18	Revision to guideline; consisting of updating position statement to include Rebinyn
03/15/18	Revision to guideline; consisting of updating position statement to include Hemlibra
04/01/18	Addition of HCPCS code C9468
05/15/18	Review and revision to guidelines; consisting of updating coding and references.
07/01/18	Addition of HCPCS code Q9995 for Hemlibra.
12/15/18	Revision to guideline; consisting of updating position statement to include Jivi (Antihemophilic Factor (Recombinant) PEGylated-aucl)
1/1/19	Revision to guideline; consisting of updating position statement
3/15/19	Revision to guideline; consisting of updating position statement
4/15/19	Revision to guideline; consisting of updating HCPCS coding
5/15/19	Review and revision to guidelines; consisting of updating position statement and references.

6/15/19	Revision to guideline; consisting of updating position statement to include Esperoct (Turoctocog alfa pegol)
7/01/19	Revision: added HCPCS code J7208
01/01/20	Update to position statement