09-J0000-34

Original Effective Date: 03/15/01

Reviewed: 05/14/25

Revised: 06/15/25

Subject: Clotting Factors and Coagulant Blood Products

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

Dosage/ Administration	Position Statement	Billing/Coding	<u>Reimbursement</u>	Program Exceptions	Definitions
<u>Related</u> Guidelines	<u>Other</u>	References	<u>Updates</u>		

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	 Bypassing agent derived from human plasma
Complex	 Contains factors II, VIIa, IX, and X
Feiba	 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	Derived from human plasma
Fibryga, RiaSTAP	• Factor I is a substrate for thrombin, factor XIIIa, and plasmin
Factor VIIa, recombinant NovoSeven, NovoSeven RT,	 Bypassing agent generated from cloned human factor VII expressed in baby hamster kidney cells
SevenFact	 Contains only activated factor VIIa
	 Short dosing interval (half-life: 3 hours)
Factor VIII	Products differ based on purity and source of factor VIII
Human: <i>Hemofil M, Monoclate-</i> P	 Facilitates the activation of factor X causing the formation of thrombin and fibrin
Recombinant: Advate, Helixate FS, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, ReFacto, Xyntha	 Factor VIII potency differs by product
Factor VIII/VWF complex	 Derived from human plasma
Alphanate, Humate P, Koate- DVI, Octanate, Wilate	 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	 Purified recombinant von Willebrand factor (rVWF) expressed in Chinese Hamster Ovary (CHO) cells
Vonvendi	 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
 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
 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 (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
 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)
 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
 BeneFIX and RIXUBIS are produced in a Chinese hamster ovary cell line

Human: AlphaNine SD,	 Mononine is purified with a murine monoclonal antibody
<i>Mononine</i> Recombinant: <i>BeneFIX,</i> <i>RIXUBIS, Ixinity</i>	• Combines with factor VIII to activate factor X (factor X converts prothrombin to thrombin; thrombin converts fibrinogen to fibrin clot)
Factor IX complex	Derived from human plasma
Bebulin, Profilnine SD	 Contains varying concentrations of factors II, VII, and X (in addition to factor IX)
Factor IX albumin fusion protein, recombinant	 Recombinant factor IX molecule is genetically fused to recombinant albumin
Idelvion	 Fusing to albumin prolongs the half-life of factor IX
Factor IX Fc fusion protein, recombinant	 Human coagulation factor IX is covalently linked to the Fc domain of human immunoglobulin G1
Alprolix	• Binding of Fc domain delays degradation to increase circulating half-life of factor IX
Factor IX GlycoPEGylated, recombinant	 Recombinant factor IX molecule is conjugated to a polyethylene glycol molecule
Rebinyn	• Conjugating to polyethylene glycol prolongs the half-life of factor IX
Coagulation Factor X, human	 Derived from human plasma
Coagadex	• 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	• Circulates in the blood and is found in platelets, macrophages,
Human: Corifact	and monocytes
Recombinant: Tretten	 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 in the past 12 months documentation from medical record must be provided, including **ALL** of the following:
 - a. Complete hematologic and musculoskeletal assessment performed by the physician
 - b. Factor replacement protocol (including dosing for both acute and prophylactic management) has been developed or evaluated by a board-certified hematologist or

hematologist-oncologist (or a physician extender practicing under their supervision) within the past 12 months

- Requested product is prescribed by a board-certified hematologist or hematologist-oncologist (or a physician extender practicing under the supervision of a hematologist or hematologistoncologist)
- 3. Member maintains a treatment log documenting any bleeds and required treatment for 12 consecutive months
 - a. Long-acting or extended half-life factor VIII and IX products a copy of the treatment log with at least 12 months of tracking bleeds must be submitted (6 months of data will be allowed if initiating therapy)
 - b. All other clotting factors and coagulant blood products a copy of the treatment log with at least 12 months of tracking bleeds must be submitted for continuation
- 4. Member meets product-specific criteria outlined in Table 2.

TABLE 2

Criteria for use of clotting factors and coagulant blood products^{1,2}

Product			equired Criteria L must be met)	Indication	Maximum Dose ²	Maximum Dispensed Quantity ²
Anti-inhibitor Coagulant Complex <i>Feiba</i>	1.		er is diagnosed with the following: Hemophilia A with high-titer factor VIII inhibitors (≥ 5	Treatment of acute bleeding episode	200 units/kg/day	5 doses
		b.	Bethesda units [BU]) – recent (within the past 90 days) laboratory documentation must be provided Hemophilia B with high-titer factor IX	Prophylaxis of post-operative bleeding ³ – documentation of planned procedure must be provided	100 units/kg x 1 dose	1 dose/procedure
			inhibitors (≥ 5 Bethesda units [BU]) – recent (within the past 90 days) laboratory documentation must be provided	Routine prophylaxis of bleeding	85 units/kg every other day	15 doses/30 days
		C.	Acquired inhibitors (≥ 5 Bethesda units [BU]) to factors VIII, XI, and XII – recent (within the past 90			

	days) laboratory documentation must be provided 2. Indication-specific dose and quantity are not exceeded ² Approval duration: 1 year			
Factor VIIa, recombinant <i>NovoSeven,</i> <i>NovoSeven RT</i>	nt one of the following: a. Hemophilia A with	Treatment of acute bleeding episode	120 mcg/kg/dose in adults or 150 mcg/kg/dose in children	5 doses
	 recent (within the past 90 days) laboratory documentation must be provided b. Hemophilia B with high-titer factor IX inhibitors (≥ 5 Bethesda units [BU]) recent (within the past 90 days) laboratory documentation must be provided Indication-specific dose and quantity are not exceeded² Approval duration: 1 year 	Prophylaxis of post-operative bleeding ³ – documentation of planned procedure must be provided	120 mcg/kg/dose in adults or 150 mcg/kg/dose in children	1 dose/procedure
	 Member is diagnosed with acquired hemophilia Indication-specific dose and quantity are not exceeded² 	Treatment of acute bleeding episode	90 mcg/kg/dose	5 doses
	Approval duration: 1 year	Prophylaxis of post-operative bleeding ³ – documentation of planned procedure must be provided	90 mcg/kg/dose	1 dose/procedure

	 Member is diagnosed with a congenital factor VII deficiency 	Treatment of acute bleeding episode	30 mcg/kg/dose	5 doses
	 Indication-specific dose and quantity are not exceeded² 			
	Approval duration: 1 year	Prophylaxis of post-operative bleeding ³ – documentation of planned procedure must be provided	30 mcg/kg/dose	1 dose/procedure
	 Member is diagnosed with Glanzmann's thrombasthenia Indication-specific dose and quantity are not exceeded² 	Treatment of acute bleeding episode	90 mcg/kg/dose	5 doses
	Approval duration: 1 year	Prophylaxis of post-operative bleeding ³ — documentation of planned procedure must be provided	90 mcg/kg/dose	1 dose/procedure
Factor VIIa, recombinant SevenFact	 Member is diagnosed with one of the following: a. Hemophilia A with high-titer factor VIII inhibitors (≥ 5 Bethesda units [BU]) – recent (within the past 90 days) laboratory documentation must be provided b. Hemophilia B with high-titer factor IX inhibitors (≥ 5 Bethesda units [BU]) – recent (within the past 90 days) laboratory 	Treatment of acute bleeding episode	225 mcg/kg x 1 dose, followed by 75 mcg/kg as needed Total daily doses not to exceed 900 mcg/kg.	5 doses (1 dose of 225 mcg/kg, 4 doses of 75 mcg/kg)

	documentation must be provided 2. Indication-specific dose and quantity are not exceeded ² Approval duration: 1 year			
Factor VIII Human: <i>Hemofil</i> <i>M, Monoclate-P</i> Recombinant: <i>Advate, Helixate</i> <i>FS, Kogenate FS,</i> <i>Kovaltry,</i> <i>Novoeight,</i> <i>Nuwiq,</i>	 Member is diagnosed with hemophilia A Member meets ONE of the following: Endogenous (baseline, not treated) factor VIII is less than or equal to 1 IU/dL (1%) – recent (within the past 90 days) 	Treatment of acute bleeding episode	50 IU/kg/dose (100 IU/kg/dose if inhibitor titers are less than 10 Bethesda units/mL)	5 doses
Recombinate, ReFacto, Xyntha	laboratory documentation must be provided b. Endogenous (baseline, not treated) factor VIII is less than or equal to 40 IU/dL (40%) AND either of the following – recent	Prophylaxis of post-operative bleeding ³ – documentation of planned procedure must be provided	50 IU/kg/dose	1 dose/procedure
	(within the past 90 days) laboratory documentation must be provided: i. Indication for use is treatment of	Routine prophylaxis of bleeding	50 IU/kg/dose three times per week or every other day	15 doses/30 days
	acute bleeding episode ii. Indication for use is prophylaxis o bleeding and member has documented history of 2 of more bleeds into large joints (i.e., ankles, knees	are less than 10 Bethesda units/mL – recent (within the past 90 days) laboratory documentation	IU/kg/day	Refer to member specific protocol

	hips, elbows, shoulders) c. Indication for use is immune tolerance induction therapy 3. Indication-specific dose and quantity are not exceeded ² Approval duration: 1 year	must be provided 2. Inhibitor titers will be measured every six months		
Factor VIII/VWF complex Alphanate, Humate P, Koate-DVI, Octanate	 Member is diagnosed with von Willebrand disease Member meets ONE of the following: Use of desmopressin is known or suspected to be ineffective or contraindicated 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 Indication-specific dose and quantity are not exceeded² 	post-operative bleeding ³ - documentation of planned	80 IU/kg/dose (Humate P) 60 IU/kg/dose (Alphanate, Humate P); 75 IU/kg/dose if age < 18 years (Alphanate)	5 doses (Humate P) 1 dose/procedure
Factor VIII/VWF complex <i>Wilate</i>	 Approval duration: 1 year Member is diagnosed with von Willebrand disease AND one the following: Member meets ONE of the following: a. Use of desmopressin is known or suspected to be ineffective or contraindicated 	Treatment of acute bleeding episode, including spontaneous bleeding or trauma induced bleeding	60 IU/kg/dose	5 doses

	· · · · · · · · · · · · · · · · · · ·		1	I
	 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 3. Indication-specific dose and quantity are not exceeded² Approval duration: 1 year 			
von Willebrand factor, recombinant	von Willebrand disease AND	Treatment of acute bleeding episode, including	80 IU/kg/dose	5 doses
Vonvendi	 Member meets ONE of the following: a. Use of desmopressin 	spontaneous bleeding or trauma induced bleeding		
Antihemophilic factor porcine, recombinant	acquired hemophilia A	Treatment of acute bleeding episode, including	200 IU/kg/dose	5 doses

Obizur	0	quantit	on-specific dose and y are not exceeded ² uration: 1 year	spontaneous bleeding or trauma induced bleeding		
Long-acting or extended half- life factor VIII products:	1. r ł 2. r	Membe hemopl Membe	<u>therapy</u> : er is diagnosed with hilia A er does not have ors to factor VIII	Treatment of acute bleeding episode	50 IU/kg/dose	5 doses Altuviiio: 2 doses
Antihemophilic factor (recombinant), single chain (Afstyla)		Membe followir a.	er meets ONE of the ng: Endogenous (baseline, not treated) factor VIII is less than or equal to 1 IU/dL (1%) – recent (within the past 90 days)	Prophylaxis of post-operative bleeding ³ documentation of planned procedure must be provided	50 IU/kg/dose Eloctate only: 60 IU/kg/dose	1 dose/procedure
Antihemophilic factor pegylated, recombinant (Adynovate)		b.	laboratory documentation must be provided Endogenous (baseline, not treated) factor VIII is less than or equal to 40 IU/dL	Routine prophylaxis of bleeding	Afstyla: 50 IU/kg/dose three times per week	Afstyla: 12 doses/30 days Adynovate, Esperoct: 14
Antihemophilic factor (recombinant), glycopegylated- exei (Esperoct) Antihemophilic factor			(40%) AND member has documented history of 2 or more bleeds into large joints (i.e., ankles, knees, hips, elbows, shoulders) – recent (within the past 90 days) laboratory documentation must be provided		Adynovate, Esperoct: 50 IU/kg/dose two times per week Jivi: 60 IU/kg/dose two times per	doses/30 days Jivi: 9 doses/30 days Eloctate: 10 doses/30 days
(recombinant) pegylated-aucl (<i>Jivi</i>) Antihemophilic factor Fc fusion protein, recombinant	i f t c c c r	is being prophyl treatme or prop operation docume	ed if requested product gused for routine laxis of bleeding (NOT ent of acute bleeding hylaxis of post- ve bleeding) – entation from the l record must be ed:		week OR 45 to 60 IU/kg/dose every 5 days Eloctate: 65 IU/kg/dose	Altuviiio: 4 doses/30 days

(rFVIIIFc) <i>(Eloctate)</i> Antihemophilic factor- recombinant, fc- vwf-xten fusion protein-ehtl Altuviiio	a. The member has had clinically evident bleeding (defined as: 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) during 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	every three to five days Altuviiio: 50 IU/kg/dose weekly
	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	
	 Indication-specific dose and quantity are not exceeded² 	
	Approval duration: 6 months	
	Continuation of therapy:	

		-	-	
	 Member meets Florida Blue's initial criteria or was previously approved by another health plan 			
	 Member demonstrates a beneficial response according to indication for use – bleed log must be provided: 			
	a. Treatment of acute bleeding episode: Bleeding episode controlled with 2 or fewer injections			
	 Routine prophylaxis of bleeding: 75% reduction in ABR 			
	 Indication-specific dose and quantity are not exceeded² 			
	Approval duration: 1 year			
Factor IX, human	 Member is diagnosed with hemophilia B 	Treatment of acute bleeding	120 IU/kg/dose	5 doses
AlphaNine SD, Mononine	 Indication-specific dose and quantity are not exceeded² 	episode	100	
	Approval duration: 1 year	Prophylaxis of post-operative bleeding ³ - documentation of planned procedure must be provided	100 IU/kg/dose	1 dose/procedure
		Routine prophylaxis of bleeding	100 IU/kg/dose two or three times per week	12 doses/30 days
Factor IX, recombinant	 Member is diagnosed with hemophilia B 	Treatment of acute bleeding	140 IU/kg/dose	5 doses
BeneFIX, Ixinity, RIXUBIS	Member meets ONE of the following:	episode Brophylaxis of	140	1
	a. Endogenous (baseline, not treated)	Prophylaxis of post-operative	140 IU/kg/dose	dose/procedure

		factor IV is loss that	blooding ³		
		factor IX is less than or equal to 1 IU/dL	bleeding ³ – documentation of		
		(1%) – recent (within			
		the past 90 days)	planned		
		laboratory	procedure must		
		documentation must	be provided		
		be provided	Routine	BeneFIX,	BeneFIX,
	b.	Endogenous	prophylaxis of	Ixfinity: 100	Ixfinity: 12
		(baseline, not treated)	bleeding	IU/kg/dose	doses/30 days
		factor IX is less than	biccomb	two or three	uoses, so uuys
		or equal to 40 IU/dL		times per	
		(40%) AND either of		week	
		the following – recent (within the past 90		WEEK	RIXUBIS: 8
		days) laboratory			doses/30 days
		documentation must			
		be provided:		RIXUBIS: 80	
		i. Indication for		IU/kg/dose	
		use is		two times per	
		treatment of		week	
		acute			
		bleeding			
		episode			
		ii. Indication for			
		use is			
		prophylaxis of			
		bleeding and			
		member has			
		documented			
		history of 2 or			
		more bleeds			
		into large			
		joints (i.e., ankles, knees,			
		hips, elbows,			
		shoulders)			
		-			
		ion-specific dose and			
	quanti	ty are not exceeded			
	Approval d	uration: 1 year			
Factor IX	1. Memb	er is diagnosed with	Treatment of	Bebulin: 120	5 doses
complex	hemop	hilia B, factor II	acute bleeding	IU/kg/dose	
		ncy, or factor X	episode	_	
Bebulin,	deficie	ncy		Profilnine SD:	
Profilnine SD				100	
				IU/kg/dose	

	2. Apj	quantit	ion-specific dose and y are not exceeded ² uration: 1 year	Prophylaxis of post-operative bleeding ³ – documentation of planned procedure must be provided	Bebulin: 120 IU/kg/dose Profilnine SD: 100 IU/kg/dose	1 dose/procedure
				Routine prophylaxis of bleeding	Bebulin: 120 IU/kg/dose Profilnine SD: 100 IU/kg/dose	8 doses/30 days
Long-acting or extended half- life factor IX products:	<u>Init</u> 1. 2.	Membe hemop Membe	<u>f therapy</u> : er is diagnosed with hilia B er does not have ors to factor IX	Treatment of acute bleeding episode	Alprolix, Idelvion: 100 IU/kg/dose Rebinyn: 80	Alprolix, Idelvion, Rebinyn: 5 doses
Factor IX albumin fusion protein, recombinant (<i>Idelvion</i>) Factor IX Fc fusion protein,	3.	Membe followi a.	Endogenous (baseline, not treated) factor IX is less than or equal to 1 IU/dL (1%) – recent (within the past 90 days) laboratory documentation must	Prophylaxis of post-operative bleeding ³ documentation of planned procedure must be provided	IU/kg/dose Alprolix, Idelvion: 100 IU/kg/dose Rebinyn: 80 IU/kg/dose	Alprolix, Idelvion, Rebinyn: 1 dose/procedure
recombinant (Alprolix) Factor IX GlycoPEGylated, recombinant (Rebinyn)		b.	be provided Endogenous (baseline, not treated) 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) – recent (within the past 90 days) laboratory documentation must be provided	Routine prophylaxis of bleeding	 Idelvion: Age 12 years and older: 40 IU/kg one time per week or 75 IU/kg every 14 days Age less than 12 years: 55 IU/kg 	4 doses/28 days

I	
 Required if requested product is being used for routine prophylaxis of bleeding (NOT treatment of acute bleeding or prophylaxis of post- operative bleeding) – documentation from the medical record must be provided: 	every 7 days Alprolix: 50 IU/kg/dose one time per week or 100 IU/kg/dose
a. The member has had clinically evident bleeding (defined as: 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) during 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:	every 10 days Rebinyn: 40 IU/kg once weekly
i. Human (plasma- derived) Factor IX (human): AlphaNine SD, Mononine ii. Factor IX,	
 Factor IX, recombinant: BeneFIX, Ixinity, RIXUBIS Indication-specific dose and quantity are not exceeded² Approval duration: 6 months 	

]
	 <u>Continuation of therapy</u>: Member meets Florida Blue's initial criteria or was previously approved by another health plan 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 Indication-specific dose and quantity are not exceeded² 			
Fibrinogen concentrate Fibryga, RiaSTAP	 Member is diagnosed with a congenital fibrinogen deficiency (e.g., afibrinogenemia, hypofibrinogenemia) that has been confirmed by blood coagulation testing Use is NOT for treatment of dysfibrinogenemia Indication-specific dose and quantity are not exceeded² Approval duration: 1 year 	Treatment of acute bleeding episode	70 mg/kg/dose unless member's baseline fibrinogen level is known	
Coagulation Factor X, human <i>Coagadex</i>	 Member is diagnosed with hereditary factor X deficiency Indication-specific dose and quantity are not exceeded² Approval duration: 1 year 	Treatment of bleeding Perioperative management of	25 IU/kg/dose one time every 24 hours 50 IU/kg/dose	

		bleeding AND member has mild hereditary factor X deficiency		
Factor XIII, human <i>Corifact</i>	 Member is diagnosed with congenital factor XIII deficiency Indication-specific dose and quantity are not exceeded² Approval duration: 1 year 	Prophylaxis of bleeding	45 IU/kg/dose every 28 days	
Factor XIII, recombinant <i>Tretten</i>	 Member is diagnosed with congenital factor XIII deficiency Indication-specific dose and quantity are not exceeded² Approval duration: 1 year 	Prophylaxis of bleeding	35 IU/kg/dose every 28 days	

- doses listed above.
- Exceptions to the listed quantity/dose will require PK studies or other medical documentation supporting clinical rationale.
- 3. Includes dental bleeding prophylaxis (e.g., tooth extraction)

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 vary 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	General dosing recommendation:
Complex	50 to 100 units/kg IV (maximum total daily dose: 200 units/kg)
Feiba	
	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	Baseline fibrinogen concentration NOT known:
Fibryga, RiaSTAP	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, recombinant 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
Factor VIIa, recombinant	Acute bleeding episodes in hemophilia A or B with inhibitors:
SevenFact	225 mcg/kg x 1 dose, then 75 mcg/kg every 2 hours until hemostasis achieved
Antihemophilic factor	General Dosing Information:
(recombinant) pegylated- aucl	Expected recovery: one unit per kilogram body weight will increase the Factor VIII level by 2 international units per deciliter (IU/dL)
Jivi	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
Factor XIII	Initial dose:
Human: <i>Corifact</i>	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.

Precautions and warnings of clotting factor and coagulant blood products		
Product	Precautions/Warnings	
Anti-inhibitor Coagulant Complex <i>Feiba</i>	Use is contraindicated in individuals with acute thrombosis, embolism, or significant signs of disseminated intravascular coagulation (DIC) (Boxed Warning)	
Fibrinogen concentrate <i>Fibryga, RiaSTAP</i>	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: <i>Hemofil M,</i> <i>Monoclate-P</i> Recombinant: <i>Advate, Helixate</i> <i>FS, Kogenate FS, Kovaltry,</i> <i>Novoeight, Nuwiq,</i> <i>Recombinate, ReFacto, Xyntha</i>	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	Use has been associated with development of factor VIII or VWF inhibitors.	

Table 4

Vonvendi	
Antihemophilic factor porcine, recombinant <i>Obizur</i>	Contraindicated in individuals with known anaphylactic or severe systemic reaction to hamster protein.
Antihemophilic factor (recombinant), single chain <i>Afstyla</i>	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) <i>Eloctate</i>	Allergic-anaphylactic reactions have been reported
Antihemophilic factor pegylated, recombinant Adynovate	Allergic-anaphylactic reactions have been reported
Antihemophilic factor (recombinant), glycopegylated- exei <i>Esperoct</i>	Allergic-anaphylactic reactions have been reported. Development of Factor VIII neutralizing antibodies can occur.
Antihemophilic factor (recombinant) pegylated-aucl <i>Jivi</i>	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.
Factor IX Human: <i>AlphaNine SD, Mononine</i> Recombinant: <i>BeneFIX,</i> <i>RIXUBIS, Ixinity</i>	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 <i>Idelvion</i>	Contraindicated in individuals with known anaphylactic or severe systemic reaction to hamster protein.
Factor IX Fc fusion protein, recombinant <i>Alprolix</i>	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	Allergic-anaphylactic reactions and thromboembolic episodes have been reported

Rebinyn	
Coagulation Factor X, human Coagadex	Hypersensitivity reactions, including anaphylaxis, are possible. Development of neutralizing antibodies (inhibitors) may occur.
Factor XIII Human: <i>Corifact</i>	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:

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 specified, 1 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), (Novoseven RT), 1 microgram
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	Injection, factor IX (antihemophilic factor, recombinant), per IU, not otherwise specified
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
J7204	Injection, factor viii, antihemophilic factor (recombinant), (esperoct), glycopegylated- exei, per 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
J7212	Factor viia (antihemophilic factor, recombinant)-jncw (Sevenfact), 1 microgram
J7213	Injection, coagulation factor ix (recombinant), Ixinity, 1 IU
J7214	Injection, factor viii/von willebrand factor complex, recombinant (Altuviiio), per factor viii 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).

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at <u>Coverage</u> <u>Protocol Exemption Request</u>.

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:

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 <u>AICC</u> AICC AICC More than 10 BU AICC AICC AICC

Guidelines to first and second choice treatment:

REFERENCES:

- 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.
- 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/.
- 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/.
- 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/."
- 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/.
- 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/.
- 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/.
- 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/.
- 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/.
- 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/.

- 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/.
- 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/.
- 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/.
- 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/.
- 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].
- 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-4113-9014c3137de0a931/.
- 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/.
- 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/.
- 28. 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
- 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/.
- 30. 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/.
- 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/Lice nsedProductsBLAs/FractionatedPlasmaProducts/UCM561316.pdf

- 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/.
- 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/.
- 34. 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/.
- 35. 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.
- 36. 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.
- 37. 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/.
- 38. Wyeth Pharmaceuticals Inc. REFACTO (antihemophilic factor (recombinant)). 2019 [cited 3/30/19]. Available from: http://www.abopharmaceuticals.com/ProductSheets/Refacto.pdf/.
- 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/.
- 40. 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/
- 41. 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 05/14/25.

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).

GUIDELINE UPDATE INFORMATION:

07/15/07	Deviewed avideline, resistein avvecation and insitetions. Defermented avideline
07/15/07	Reviewed guideline: maintain current coverage and limitations. Reformatted guideline,
01/01/00	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
01/01/00	coding and updated references and links.
01/01/09	Annual HCPCS coding update: deleted 90765 and 90766; added J7186, 96365 and
07/04/00	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 of 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 guideline 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).
01/01/19	Revision to guideline; consisting of updating position statement.
03/15/19	Revision to guideline; consisting of updating position statement.
04/15/19	Revision to guideline; consisting of updating HCPCS coding.
05/15/19	Review and revision to guidelines; consisting of updating position statement and
	references.
06/15/19	Revision to guideline; consisting of updating position statement to include Esperoct
	(Turoctocog alfa pegol).
07/01/19	Revision: added HCPCS code J7208.
01/01/20	Update to position statement.
07/15/20	Revision to position statement.
11/15/20	Revision to position statement.
01/01/21	Revision: Added HCPCS code J7212 and revised description on code J7189.
03/15/23	Revision to position statement to include Rebinyn prophylaxis dosing.
07/01/23	Review and revision to guideline. Addition of Altuviiio. Addition of HCPCS code J7213.
10/01/23	Revision: Added HCPCS code J7214.
04/01/24	Revision: Removed Hemlibra from Medical Coverage Guideline.
06/15/25	Revision to position statement.