Antihemophilic and Clotting Factors

Override(s)	Approval Duration
Prior Authorization	1 year

Medications
ADVATE
Adynovate
Afstyla
Alphanate
AlphaNine SD
Alprolix
Altuviiio
BeneFix
Coagadex
Corifact
Eloctate
Esperoct
FEIBA
Fibryga
Hemlibra
HEMOFIL M
HUMATE-P
Idelvion
Ixinity
Jivi
Koate
Koate-DVI
Kogenate FS
Kovaltry
Mononine
Novoeight

NovoSeven RT
Nuwiq
Obizur
Profilnine SD
Rebinyn
RECOMBINATE
RiaSTAP
RIXUBIS
SevenFact
TRETTEN
Vonvendi
Wilate
Xyntha
Xyntha Solufuse

APPROVAL CRITERIA

FEIBA (Anti-inhibitor Coagulant Complex)

Initial requests for FEIBA (Anti-inhibitor Coagulant Complex) may be approved if the following criteria are met:

I. Individual has a diagnosis of hemophilia A or B with inhibitors to Factor VIII or Factor IX; **AND**
II. Individual is using for one of the following:
   A. Treatment of bleeding episodes; **OR**
   B. Peri-procedural operative management for surgical, invasive or interventional radiology procedures; **OR**
   C. Routine prophylaxis to prevent or reduce the frequency of bleeding episodes.

Continuation requests for FEIBA (Anti-inhibitor Coagulant Complex) may be approved if the following criteria are met:

I. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

Feiba (Anti-inhibitor Coagulant Complex) may not be approved for the following:

I. Individual is using to treat bleeding episodes resulting from coagulation factor deficiencies in the absence of inhibitors to coagulation Factor VIII or coagulation Factor IX; **OR**
II. When the above criteria are not met and for all other indications.

Note: FEIBA (anti-inhibitor coagulant complex) has a black box warning for thromboembolic events, particularly following the administration of high doses and/or in individuals with thrombotic risk factors.

NovoSeven RT (Factor VIIa Recombinant)

Initial requests for NovoSeven RT (Factor VIIa recombinant) may be approved if the following criteria are met:

I. Individual has one of the following diagnoses:
   A. Hemophilia A or B with inhibitors to Factor VIII or Factor IX; **OR**
   B. Acquired hemophilia; **OR**
   C. Congenital Factor VII deficiency;

AND

II. Individual is using for one of the following:
   A. Treatment of bleeding episodes; **OR**
   B. Prevention of bleeding in surgical interventions or invasive procedures.

OR

III. Individual has a diagnosis of Glansmann's thrombasthenia; **AND**
IV. Individual is using for the treatment of bleeding episodes and peri-operative management related to diagnosis; **AND**
V. Individual has documented refractoriness to platelet transfusions with or without antibodies to platelets;

Continuation requests for NovoSeven RT (Factor VIIa recombinant) may be approved if the following criteria are met:

I. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

NovoSeven RT (Factor VIIa recombinant) may not be approved when the above criteria are not met and for all other indications.

Note: NovoSeven, NovoSeven RT [coagulation Factor VIIa (recombinant)] have a black box warning for thromboembolic events, particularly after high doses and/or in patients with thrombotic risk factors.

SevenFact (Factor VIIa Recombinant)

Initial requests for SevenFact (Factor VIIa Recombinant) may be approved if the following criteria are met:

I. Individual is 12 years of age or older; **AND**
II. Individual has a diagnosis of hemophilia A or B with inhibitors to Factor VIII or Factor IX; **AND**
III. Individual is using for the treatment and control of bleeding episodes.

Continuation requests for SevenFact (Factor VIIa Recombinant) may be approved if the following criteria are met:

I. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

SevenFact (Factor VIIa Recombinant) may not be approved for the following:

I. Individual is using for the treatment of congenital factor VII deficiency; **OR**
II. Individual is using to treat bleeding episodes resulting from coagulation factor deficiencies in the absence of inhibitors to coagulation Factor VIII or coagulation Factor IX; **OR**
III. When the above criteria are not met and for all other indications.

Note: SevenFact [coagulation Factor VIIa (recombinant)] has a black box warning for thromboembolic events, particularly after high doses and/or in patients with thrombotic risk factors.

Hemofil M, Koate-DVI (Factor VIII Human plasma-derived)

Initial requests for Hemofil M or Koate/Koate-DVI (Factor VIII, human plasma-derived) may be approved if the following criteria are met:

I. Individual has a diagnosis of hemophilia A (also called factor VIII deficiency or classic hemophilia); **AND**
II. Individual is using for the treatment of bleeding episodes;

OR

III. Individual has a diagnosis of hemophilia A (also called factor VIII deficiency or classic hemophilia); **AND**
IV. Individual is using as routine prophylaxis to prevent or reduce the frequency of bleeding episodes; **AND**
V. Individual has a diagnosis of severe hemophilia A (defined as less than 1 International Unit per deciliter [1IU/dL] or 1% endogenous Factor VIII) (NHF, Srivastava 2020);

OR

VI. Individual has a diagnosis of hemophilia A (also called factor VIII deficiency or classic hemophilia); **AND**
VII. Individual is using as routine prophylaxis to prevent or reduce the frequency of bleeding episodes; **AND**
VIII. Individual has a diagnosis of mild to moderate hemophilia A (defined as endogenous Factor VIII less than 40 IU/dL [less than 40%], but greater than or equal to 1 IU) (NHF, Srivastava 2020); **AND**
IX. Individual has one of the following (NHF, Srivastava 2020):
    A. One or more episodes of spontaneous bleeding into joint; **OR**
    B. One or more episodes of severe, life-threatening, or spontaneous bleeding as determined by the prescriber; **OR**
    C. Severe phenotype hemophilia determined by the individual's risk factors that increase the risk of a clinically significant bleed, including but not limited to, participation in activities likely to cause injury/trauma, procoagulant and anticoagulant protein levels, comorbid conditions affecting functional ability and physical coordination, or history of a clinically significant bleed.

Initial requests for Koate/Koate-DVI (Factor VIII, human plasma-derived) may be approved if the following criteria are met:

I. Individual has a diagnosis of hemophilia A (also called factor VIII deficiency or classic hemophilia); **AND**
II. Individual is using for peri-procedural management for surgical, invasive or interventional radiology procedures.

Continuation requests for Hemofil M or Koate/Koate-DVI (Factor VIII, human plasma-derived) may be approved if the following criteria are met:

I. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

Hemofil M or Koate/Koate-DVI (Factor VIII, human plasma-derived) may not be approved for the following:

I. Individual is using for the treatment of von Willebrand disease (VWD); **OR**
II. When the above criteria are not met and for all other indications.

<u>Advate, Afstyla, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, Xyntha/Xyntha Solofuse (Factor VIII Recombinant)</u>

Initial requests for Advate, Afstyla, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, or Xyntha/Xyntha Solofuse (Factor VIII recombinant) may be approved if the following criteria are met:

I. Individual has a diagnosis of hemophilia A (also called factor VIII deficiency or classic hemophilia);

AND

II. Individual is using for one of the following:
   A. Treatment of bleeding episodes; **OR**
   B. Peri-procedural management for surgical, invasive or interventional radiology procedures;

OR

III. Individual has a diagnosis of von Willebrand disease (VWD); **AND**
IV. Individual is using for the treatment of bleeding episodes; **AND**
V. Individual is using in combination with Vonvendi (recombinant von Willebrand factor complex); **AND**
VI. Individual has a baseline factor VIII level less than 40 IU/dL [less than 40%] or are unknown (Vonvendi 2018).

OR

VII. Individual has a diagnosis of von Willebrand disease (VWD); **AND**
VIII. Individual is using for peri-procedural management for surgical, invasive or interventional radiology procedures; **AND**
IX. Individual is using in combination with Vonvendi (recombinant von Willebrand factor complex); **AND**
X. Individual has a baseline factor VIII level less than 30 IU/dL [less than 30%] or are unknown (Vonvendi 2018).

Initial requests for Advate, Afstyla, Kogenate FS, Kovaltry, Novoeight, Nuwiq, or Xyntha/Xyntha Solofuse (Factor VIII recombinant) may be approved if the following criteria are met:

I. Individual is using as routine prophylaxis to prevent or reduce the frequency of bleeding episodes; **AND**
II. Individual has a diagnosis of severe hemophilia A (defined as less than 1 International Unit per deciliter [1IU/dL] or 1% endogenous Factor VIII) (NHF, Srivastava 2020);

OR

III. Individual has mild to moderate hemophilia A (defined as endogenous Factor VIII less than 40 IU/dL [less than 40%], but greater than or equal to 1 IU) (NHF, Srivastava 2020); **AND**
IV. Individual is using as routine prophylaxis to prevent or reduce the frequency of bleeding episodes; **AND**
V. Individual has one of the following:
   A. One or more episodes of spontaneous bleeding into joint; **OR**
   B. One or more episodes of severe, life-threatening, or spontaneous bleeding as determined by the prescriber ; **OR**

C. Severe phenotype hemophilia determined by the individual's risk factors that increase the risk of a clinically significant bleed, including but not limited to, participation in activities likely to cause injury/trauma, procoagulant and anticoagulant protein levels, comorbid conditions affecting functional ability and physical coordination, or history of a clinically significant bleed.

Initial requests for Kogenate FS (Factor VIII recombinant) may be approved if the following criteria are met:

I. Individual is 16 years of age or younger; **AND**
II. Individual has a diagnosis of hemophilia A (also called factor VIII deficiency or classic hemophilia); **AND**
III. Individual is using as routine prophylaxis to reduce the risk of joint damage in those without pre-existing joint damage.

Initial requests for Recombinate (Factor VIII recombinant) may be approved if the following criteria are met:

I. Individual is using for the treatment of acquired Factor VIII inhibitors not exceeding 10 Bethesda Unit (BU) per milliliter (mL).

Continuation requests for Advate, Afstyla, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, or Xyntha/Xyntha Solofuse (Factor VIII recombinant) may be approved if the following criteria are met:

I. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

Advate, Afstyla, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, or Xyntha/Xyntha Solofuse (Factor VIII recombinant) may not be approved for the following:

I. Individual is using as monotherapy for the maintenance treatment of von Willebrand disease (VWD); **OR**
II. When the above criteria are not met and for all other indications.

Long Acting Agents [Adynovate (Factor VIII Long-Acting Recombinant, pegylated), Jivi (Factor VIII Recombinant, PEGylated damactocog alfa pegol), Eloctate (Factor VIII Recombinant Anti-hemophilic Factor Fc Fusion Protein), Esperoct (Factor VIII Recombinant, glycopegylated), or Factor VIII Recombinant Antihemophilic Factor FC-VWF-XTEN Fusion Protein (Altuviiio)]

Initial requests for Adynovate (Factor VIII Long-Acting Recombinant, pegylated), Jivi (Factor VIII Recombinant PEGylated damactocog alfa pegol), Eloctate (Factor VIII Recombinant Anti-hemophilic Factor Fc Fusion Protein), Esperoct (Factor VIII Recombinant, glycopegylated), or

Factor VIII Recombinant Antihemophilic Factor FC-VWF-XTEN Fusion Protein (Altuviiio) may be approved if the following criteria are met:

I. Individual has a diagnosis of severe hemophilia A (defined as less than 1 International Unit per deciliter [1IU/dL] endogenous factor VIII) (NHF, Srivastava 2020); **AND**
II. Individual is using for one of the following:
    A. Treatment of acute bleeding episodes; **OR**
    B. Peri-procedural management for surgical, invasive or interventional radiology procedures; **OR**
    C. Routine prophylaxis to prevent or reduce the frequency of bleeding episodes;

AND

III. If using Jivi, individual is 12 years of age or older and has been previously treated with factor VIII;

OR

IV. Individual has a diagnosis of mild to moderate hemophilia A (defined as endogenous factor VIII less than 40 IU/dl [less than 40%], but greater than or equal to 1 IU) (NHF, Srivastava 2020); **AND**
V. Individual is using for one of the following:
    A. Treatment of acute bleeding episodes; **OR**
    B. Peri-procedural management for surgical, invasive or interventional radiology procedures; **OR**
    C. Routine prophylaxis to prevent or reduce the frequency of bleeding episodes when one of the following:
        1. Individual has had one or more episodes of spontaneous bleeding into joint; **OR**
        2. Individual has had one or more episodes of severe, life-threatening, or spontaneous bleeding as determined by the prescriber; **OR**
        3. Severe phenotype hemophilia determined by the individual's risk factors that increase the risk of a clinically significant bleed, including but not limited to, participation in activities likely to cause injury/trauma, procoagulant and anticoagulant protein levels, comorbid conditions affecting functional ability and physical coordination, or history of a clinically significant bleed;

AND

VI. If using Jivi, individual is 12 years of age or older and has been previously treated with factor VIII.

Continuation requests for Adynovate (Factor VIII Long-Acting Recombinant, pegylated), Jivi (Factor VIII Recombinant PEGylated damactocog alfa pegol), Eloctate (Factor VIII Recombinant Anti-hemophilic Factor Fc Fusion Protein), Esperoct (Factor VIII Recombinant, glycopegylated), or Factor VIII Recombinant Antihemophilic Factor FC-VWF-XTEN Fusion Protein (Altuviiio) may be approved if the following criteria are met:

I. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

Adynovate (Factor VIII Long-Acting Recombinant, pegylated), Jivi (Factor VIII Recombinant PEGylated damactocog alfa pegol), Eloctate (Factor VIII Recombinant Anti-hemophilic Factor Fc Fusion Protein), Esperoct (Factor VII Recombinant, glycopegylated), or Factor VIII Recombinant Antihemophilic Factor FC-VWF-XTEN Fusion Protein (Altuviiio) may not be approved for the following:

I. Individual is using for the treatment of von Willebrand disease; **OR**
II. When the above criteria are not met and for all other indications.

Hemlibra (emicizumab) - Anti-hemophilic bispecific factor - Factor IXa and Factor X Prior Authorization

Initial requests for Hemlibra (emicizumab-kxwh) may be approved if the following criteria are met:

I. Individual has a diagnosis of severe hemophilia A (defined as less than 1 International Unit per deciliter [1IU/dL] endogenous factor VIII) (NHF, Srivastava 2020); **AND**
II. Individual is using for routine prophylaxis to prevent or reduce the frequency of bleeding episodes; **AND**
III. Individual has one of the following:
    A. If switching from factor VIII agents, then individual will discontinue factor VIII agents being used for routine prophylaxis after the first week of Hemlibra initiation; **OR**
    B. If switching from bypassing agents (i.e., NovoSeven RT, SevenFact, FEIBA), then individual will discontinue bypassing agents being used for routine prophylaxis after 24 hours of Hemlibra initiation;

OR

IV. Individual has a diagnosis of mild to moderate hemophilia A (defined as endogenous Factor VIII less than 40 IU/dl [less than 40%], but greater than or equal to 1 IU/dl) (NHF, Srivastava 2020); **AND**
V. Individual is using for routine prophylaxis to prevent or reduce the frequency of bleeding episodes; **AND**
VI. Individual has one of the following:
    A. One or more episodes of spontaneous bleeding into joint; **OR**
    B. One or more episodes of severe, life-threatening, or spontaneous bleeding as determined by the prescriber;
    OR
    C. Severe phenotype hemophilia determined by the individual's risk factors that increase the risk of a clinically significant bleed, including but not limited to, participation in activities likely to cause injury/trauma, procoagulant and anticoagulant protein levels, comorbid conditions affecting functional ability and physical coordination, or history of a clinically significant bleed; **AND**

VII. Individual has one of the following:

A. If switching from factor VIII agents, then individual will discontinue factor VIII agents being used for routine prophylaxis after the first week of Hemlibra initiation; **OR**
B. If switching from bypassing agents (i.e., NovoSeven RT, SevenFact, FEIBA), then individual will discontinue bypassing agents being used for routine prophylaxis after 24 hours of Hemlibra initiation.

Continuation requests for Hemlibra (emicizumab-kxwh) may be approved if the following criteria are met:

I. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

Hemlibra (emicizumab-kxwh) may not be approved when the above criteria are not met and for all other indications.

Note: Hemlibra has a black box warning for thrombotic microangiopathy and thromboembolism, especially when administered with activated prothrombin complex concentrate (aPCC).

Obizur (Factor VIII Recombinant, Porcine Sequence)

Initial requests for Obizur (Recombinant, Porcine Sequence) may be approved if the following criteria are met:

I. Individual is 18 years of age or older; **AND**
II. Individual has a diagnosis of acquired hemophilia A; **AND**
III. Individual has baseline anti-porcine Factor VIII inhibitor titer less than or equal to 20 BU/mL; **AND**
IV. Individual is using for the treatment and control of bleeding episodes.

Continuation requests for Obizur (Recombinant, Porcine Sequence) may be approved if the following criteria are met:

I. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

Obizur (Recombinant, Porcine Sequence) may not be approved for the following:

I. Individual has a diagnosis of congenital hemophilia A with Factor VIII deficiency; **OR**
II. Individual has a diagnosis of congenital hemophilia A with inhibitors; **OR**
III. Individual has a diagnosis of von Willebrand disease; **OR**
IV. When the above criteria are not met and for all other indications.

Alphanate, Humate-P, Wilate (Anti-hemophilic Factor VIII/von Willebrand Factor Complex, Human)

Initial requests for Alphanate, Humate-P, or Wilate (Anti-hemophilic Factor VIII/von Willebrand Factor Complex, Human) may be approved if the following criteria are met:

I. Individual has a diagnosis of severe von Willebrand disease (VWD); **OR**
II. Individual has a diagnosis of mild to moderate VWD and use of desmopressin is known or suspected to be inadequate;

AND

III. Individual is using for one of the following:
    A. The treatment of spontaneous or trauma-induced bleeding episodes; **OR**
    B. Peri-procedural management for surgical, invasive or interventional radiology procedures.

Initial requests for Alphanate, Humate-P, or Wilate (Anti-hemophilic Factor VIII/von Willebrand Factor Complex, Human) may be approved if the following criteria are met:

I. Individual has a diagnosis of hemophilia A (also called factor VIII deficiency or classic hemophilia); **AND**
II. Individual is using for the treatment of bleeding episodes;

OR

III. Individual has a diagnosis of severe hemophilia A (defined as less than 1 International Unit per deciliter [1IU/dL] endogenous Factor VIII) (NHF, Srivastava 2020); **AND**
IV. Individual is using for routine prophylaxis to prevent or reduce the frequency of bleeding episodes;

OR

V. Individual has a diagnosis of mild to moderate hemophilia A (defined as endogenous Factor VIII less than 40 IU/dL [less than 40%], but greater than or equal to 1 IU) (NHF, Srivastava 2020); **AND**
VI. Individual is using for routine prophylaxis to prevent or reduce the frequency of bleeding episodes when there is one of the following:
    A. Individual has had one or more episodes of spontaneous bleeding into joint; **OR**
    B. Individual has had one or more episodes of severe, life-threatening, or spontaneous bleeding as determined by the prescriber; **OR**
    C. Severe phenotype hemophilia determined by the individual's risk factors that increase the risk of a clinically significant bleed, including but not limited to, participation in activities likely to cause injury/trauma, procoagulant and anticoagulant protein levels, comorbid conditions affecting functional ability and physical coordination, or history of a clinically significant bleed.

Initial requests for Alphanate (Anti-hemophilic Factor VIII/von Willebrand Factor Complex, Human) may be approved if the following criteria are met:

I. Individual has a diagnosis of acquired Factor VIII deficiency; **AND**
II. Individual is using for the treatment of bleeding episodes.

Continuation requests for Alphanate, Humate-P, or Wilate (Anti-hemophilic Factor VIII/von Willebrand Factor Complex, Human) may be approved if the following criteria are met:

I. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

Alphanate (Anti-hemophilic Factor VIII/von Willebrand Factor Complex, Human) may not be approved for the following:

I. Individual has a diagnosis for severe (type 3) von Willebrand disease; **AND**
II. Individual is undergoing major surgery;

OR
III. Individual is using for prophylaxis of spontaneous bleeding episodes in von Willebrand disease.

Humate-P and Wilate (Anti-hemophilic Factor VIII/von Willebrand Factor Complex, Human) may not be approved for the following:

I. Individual is using for prophylaxis of spontaneous bleeding episodes in von Willebrand disease.

Alphanate, Humate-P, Wilate (Anti-hemophilic Factor VIII/von Willebrand Factor Complex, Human) may not be approved when the above criteria are not met and for all other indications.

Vonvendi (Recombinant von Willebrand Factor Complex)

Initial requests for Vonvendi (Recombinant von Willebrand Factor Complex) may be approved if the following criteria are met:

I. Individual is 18 years of age or older; **AND**
II. Individual is using for one of the following:
    A. Individual has a diagnosis of severe von Willebrand disease (VWD); **OR**
    B. Individual has a diagnosis of mild to moderate VWD and use of desmopressin is known or suspected to be inadequate;

AND
III. Individual is using for one of the following:
    A. Individual is using to treat spontaneous or trauma-induced bleeding episodes, or for peri-procedural management for surgical, invasive or interventional radiology procedures; OR

B. Individual is using as routine prophylaxis to prevent or reduce the frequency of bleeding episodes receiving on-demand therapy.

Continuation requests for Vonvendi (Recombinant von Willebrand Factor Complex) may be approved if the following criteria are met:

I. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

Vonvendi (Recombinant von Willebrand Factor Complex) may not be approved when the above criteria are not met and for all other indications.

Alphanine SD or Mononine (Human plasma-derived, Coagulation Factor IX)

Initial requests for Alphanine SD or Mononine (Human plasma derived, Coagulation Factor IX) may be approved if the following criteria are met:

I. Individual has a diagnosis of hemophilia B (also called factor IX deficiency or Christmas disease); **AND**
II. Individual is using for the treatment of bleeding episodes;

OR

III. Individual has a diagnosis of severe hemophilia B (defined as less than 1 IU/dL or 1% endogenous Factor IX) (NHF, Srivastava 2020);
AND
IV. Individual is using for routine prophylaxis to prevent or reduce the frequency of bleeding episodes;

OR

V. Individual has a diagnosis of mild to moderate hemophilia B (defined as endogenous Factor IX less than 40 IU/dL [less than 40%], but greater than or equal to 1 IU/dL) (NHF, Srivastava 2020); **AND**
VI. Individual is using for routine prophylaxis to prevent or reduce the frequency of bleeding episodes; **AND**
VII. Individual has one of the following:
   A. One or more episodes of spontaneous bleeding into joint; **OR**
   B. One or more episodes of severe, life-threatening, or spontaneous bleeding as determined by the prescriber; **OR**
   C. Severe phenotype hemophilia determined by the individual's risk factors that increase the risk of a clinically significant bleed, including but not limited to, participation in activities likely to cause injury/trauma, procoagulant and anticoagulant protein levels, comorbid conditions affecting functional ability and physical coordination, or history of a clinically significant bleed.

Continuation requests for Alphanine SD or Mononine (Human plasma derived, Coagulation Factor IX) may be approved if the following criteria are met:

I. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

Alphanine SD or Mononine (Human plasma derived, Coagulation Factor IX) may not be approved for the following:

I. Treatment or reversal of coumarin-induced anticoagulation; **OR**
II. Hemorrhagic state or coagulopathy associated with liver dysfunction; **OR**
III. Treatment of individuals with hemophilia A with inhibitors to factor VIII; **OR**
IV. Replacement therapy of other clotting factors which include factors II, VII, and X; **OR**
V. When the above criteria are not met and for all other indications.

<u>Profilnine SD (Human plasma-derived, Factor IX Complex)</u>

Initial requests for Profilnine SD (Human plasma-derived, Factor IX Complex) may be approved if the following criteria are met:

I. Individual has a diagnosis of hemophilia B (also called factor IX deficiency or Christmas disease); **AND**
II. Individual is using for the treatment of bleeding episodes;

OR

III. Individual has a diagnosis of severe hemophilia B (defined as less than 1 IU/dL or 1% endogenous Factor IX) (NHF 2016 update, Srivastava 2013); **AND**
IV. Individual is using as routine prophylaxis to prevent or reduce the frequency of bleeding episodes;

OR

V. Individual has a diagnosis of mild to moderate hemophilia B (defined as endogenous Factor IX less than 40 IU/dL [less than 40%], but greater than or equal to 1 IU/dL) NHF, Srivastava 2020); **AND**
VI. Individual is using for routine prophylaxis to prevent or reduce the frequency of bleeding episodes;
AND
VII. Individual has one of the following:
    A. One or more episodes of spontaneous bleeding into joint; **OR**
    B. One or more episodes of severe, life-threatening, or spontaneous bleeding as determined by the prescriber; **OR**
    C. Severe phenotype hemophilia determined by the individual's risk factors that increase the risk of a clinically significant bleed, including but not limited to, participation in activities likely to cause injury/trauma, procoagulant and anticoagulant protein levels, comorbid conditions affecting functional ability and physical coordination, or history of a clinically significant bleed.

Continuation requests for Profilnine SD (Human plasma-derived, Factor IX Complex) may be approved if the following criteria are met:

I. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

Profilnine SD (Human plasma-derived, Factor IX Complex) may not be approved for the following:

I. Individual has a diagnosis of Factor VII deficiency; **OR**
II. When the above criteria are not met and for all other indications.

Benefix, Ixinity, or Rixubis (Recombinant Factor IX)

Initial requests for Benefix, Ixinity, or Rixubis (Recombinant Factor IX) may be approved if the following criteria are met:

I. Individual has a diagnosis of hemophilia B (also called factor IX deficiency or Christmas disease); **AND**
II. Individual is using for one of the following:
    A. Individual is using for the treatment of bleeding episodes; **OR**
    B. Individual is using for peri-procedural management for surgical, invasive or interventional radiology procedures;

OR

III. Individual has a diagnosis of severe hemophilia B (defined as less than 1 IU/dL or 1% endogenous Factor IX) (NHF, Srivastava 2020); **AND**
IV. Individual is using as routine prophylaxis to prevent or reduce the frequency of bleeding episodes;

OR

V. Individual has a diagnosis of mild to moderate hemophilia B (defined as endogenous Factor IX less than 40 IU/dL [less than 40%], but greater than or equal to 1 IU/dL) (NHF, Srivastava 2020); **AND**
VI. Individual is using for routine prophylaxis to prevent or reduce the frequency of bleeding episodes;
AND
VII. Individual has one of the following:
    A. One or more episodes of spontaneous bleeding into joint; **OR**
    B. One or more episodes of severe, life-threatening, spontaneous bleeding as determined by the prescriber; **OR**
    C. Severe phenotype hemophilia determined by the individual's risk factors that increase the risk of a clinically significant bleed, including but not limited to, participation in activities likely to cause injury/trauma, procoagulant and

anticoagulant protein levels, comorbid conditions affecting functional ability and physical coordination, or history of a clinically significant bleed.

Continuation requests for Benefix, Ixinity, Rixubis (Recombinant Factor IX) may be approved if the following criteria are met:

I. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

Benefix, Ixinity, Rixubis (Recombinant Factor IX) may not be approved for the following:

I. Treatment of other factor deficiencies (for example factors II, VII, VIII and X); **OR**
II. Treatment of individuals with hemophilia A with inhibitors to factor VIII; **OR**
III. To reverse coumarin-induced anticoagulation; **OR**
IV. Treatment of bleeding due to low levels of liver-dependent coagulation factors; **OR**
V. Using for the induction of immune tolerance in individuals with hemophilia B; **OR**
VI. When the above criteria are not met and for all other indications.

Idelvion (Recombinant Long-Acting, Albumin Fusion Protein Coagulation Factor IX), Alprolix (Recombinant, Fc Fusion Protein Coagulation Factor IX), or Rebinyn (Recombinant, glycoPEGylated Coagulation Factor IX)

Initial requests for Idelvion (Recombinant Long-Acting, Albumin Fusion Protein Coagulation Factor IX), Alprolix (Recombinant, Fc Fusion Protein Coagulation Factor IX), or Rebinyn (Recombinant, glycoPEGylated Coagulation Factor IX) may be approved if the following criteria are met:

I. Individual has a diagnosis of severe hemophilia B (also called factor IX deficiency or Christmas disease); **AND**
II. Individual has less than 1 IU/dL (less than 1%) endogenous Factor IX (NHF, Srivastava 2020); **AND**
III. Individual is using for one of the following:
    A. The treatment of bleeding episodes; **OR**
    B. Peri-procedural management for surgical, invasive or interventional radiology procedures; **OR**
    C. Routine prophylaxis to prevent or reduce the frequency of bleeding episodes;

OR

IV. Individual has a diagnosis of mild to moderate hemophilia B; **AND**
V. Individual has endogenous Factor IX level less than 40 IU/dL (less than 40%) but greater than or equal to 1 IU/dL (NHF, Srivastava 2020); **AND**
VI. Individual is using for one of the following:
    A. Individual is using for the treatment of bleeding episodes; **OR**
    B. Individual is using for peri-procedural management for surgical, invasive or interventional radiology procedures; **OR**

C. Individual is using for routine prophylaxis to prevent or reduce the frequency of bleeding episodes when there is one of the following:
    1. Individual has had one or more episodes of spontaneous bleeding into joint; **OR**
    2. Individual has had one or more episodes of severe, life-threatening, or spontaneous bleeding as determined by the prescriber; **OR**
    3. Severe phenotype hemophilia determined by the individual's risk factors that increase the risk of a clinically significant bleed, including but not limited to, participation in activities likely to cause injury/trauma, procoagulant and anticoagulant protein levels, comorbid conditions affecting functional ability and physical coordination, or history of a clinically significant bleed.

Continuation requests for Idelvion (Recombinant Long-Acting, Albumin Fusion Protein Coagulation Factor IX), Alprolix (Recombinant, Fc Fusion Protein Coagulation Factor IX), or Rebinyn (Recombinant, glycoPEGylated Coagulation Factor IX) may be approved if the following criteria are met:

I. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

Idelvion (Recombinant Long-Acting, Albumin Fusion Protein Coagulation Factor IX), Alprolix (Recombinant, Fc Fusion Protein Coagulation Factor IX), or Rebinyn (Recombinant, GlycoPEGylated Coagulation Factor IX) may not be approved for the following:

I. Using for the induction of immune tolerance in individuals with hemophilia B; **OR**
II. When the above criteria are not met and for all other indications.

<u>Coagadex (Human-plasma derived Coagulation Factor X)</u>

Initial requests for Coagadex (Human-plasma derived Coagulation Factor X) may be approved if the following criteria are met:

I. Individual has a diagnosis of severe or moderate hereditary Factor X deficiency (defined as less than 5 IU/dL or 5% endogenous Factor X) (NHF, Srivastava 2020); **AND**
II. Individual is using for one of the following:
    A. Treatment of acute bleeding episodes; **OR**
    B. Peri-procedural management for surgical, invasive or interventional radiology procedures; **OR**
    C. Routine prophylaxis to prevent or reduce the frequency of bleeding episodes;

OR

III. Individual has a diagnosis of mild hereditary Factor X deficiency (defined as greater than or equal to 5 IU/dL or 5% endogenous Factor X) (NHF, Srivastava 2020); **AND**

IV. Individual is using for one of the following:
    A. Treatment of acute bleeding episodes; **OR**
    B. Peri-procedural management for surgical, invasive or interventional radiology procedures; **OR**
    C. Routine prophylaxis to prevent or reduce the frequency of bleeding episodes when there is one of the following:
        1. One or more episodes of spontaneous bleeding into joint; **OR**
        2. One or more episodes of severe, life-threatening, or spontaneous bleeding as determined by the prescriber; **OR**
        3.
        4. Severe phenotype hemophilia determined by the individual's risk factors that increase the risk of a clinically significant bleed, including but not limited to, participation in activities likely to cause injury/trauma, procoagulant and anticoagulant protein levels, comorbid conditions affecting functional ability and physical coordination, or history of a clinically significant bleed.

Continuation requests for Coagadex (Human-plasma derived Coagulation Factor X) may be approved if the following criteria are met:

I. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

Coagadex (Human-plasma derived Coagulation Factor X) may not be approved for the following:

I. Individual with severe hereditary Factor X deficiency is using for perioperative management of bleeding in major surgery; **OR**
II. When the above criteria are not met and for all other indications.

<u>Tretten or Corifact (Factor XIII)</u>

Initial requests for Corifact (Human Plasma-derived, Factor XIII) may be approved if the following criteria are met:

I. Individual has a diagnosis of Factor XIII deficiency;
AND
II. Individual is using for routine prophylactic treatment to prevent or reduce the frequency of bleeding episodes; **OR**
III. Individual is using for peri-procedural management for surgical, invasive or interventional radiology procedures.

Initial requests for Tretten (Recombinant Factor XIII A-Subunit) may be approved if the following criteria are met:

I. Individual has a diagnosis of congenital Factor XIII A-Subunit deficiency; **AND**

II. Individual is using as routine prophylaxis for bleeding.

Continuation requests for Corifact (Human Plasma-derived, Factor XIII) or Tretten (Recombinant Factor XIII A-Subunit) may be approved if the following criteria are met:

I. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

Corifact (Human Plasma-derived, Factor XIII) may not be approved for the following:

I. When the above criteria are not met and for all other indications.

Tretten (Recombinant Factor XIII A-Subunit) may not be approved for the following:

I. Individual with congenital Factor XIII B-subunit deficiency; **OR**
II. When the above criteria are not met and for all other indications.

RiaSTAP (Human plasma-derived Fibrinogen concentrate) or Fibryga (Human fibrinogen)

Initial requests for RiaSTAP (Human plasma-derived Fibrinogen concentrate) or Fibryga (Human fibrinogen) may be approved if the following criteria are met:

I. Individual has a diagnosis of congenital fibrinogen deficiency (afibrinogenemia or hypofirbinogenemia); **AND**
II. Individual is using for the treatment of acute bleeding episodes.

Continuation requests for RiaSTAP (Human plasma-derived Fibrinogen concentrate) or Fibryga (Human fibrinogen) may be approved if the following criteria are met:

I. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

RiaSTAP (Human plasma-derived Fibrinogen concentrate) or Fibryga (Human fibrinogen) may not be approved for the following:

I. Individual has a diagnosis of dysfibrinogenemia; **OR**
II. When the above criteria are not met and for all other indications.

Key References:

1. Centers for Disease Control and Prevention. Hemophilia Facts. Available at: http://www.cdc.gov/ncbddd/hemophilia/facts.html.

2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2023. URL: http://www.clinicalpharmacology.com. Updated periodically.
3. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Updated periodically.
4. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
5. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2023; Updated periodically.
6. National Hemophilia Foundation (NHF). Available at: http://www.hemophilia.org/. Accessed on October 2, 2023.
7. National Hemophilia Foundation (NHF). Recommendations Concerning Products Licensed for the Treatment of Hemophilia and Other Bleeding Disorders. January 2021. Available at https://www.hemophilia.org/Researchers-Healthcare-Providers/Medical-and-Scientific-Advisory-Council-MASAC/MASAC-Recommendations/MASAC-Recommendations-Concerning-Products-Licensed-for-the-Treatment-of-Hemophilia-and-Other-Bleeding-Disorders. Accessed on September 29, 2023.
8. National Hemophilia Foundation (NHF). Recommendation on the Use and Management of Emicizumab-kxwh (Hemlibra) for Hemophilia A with and without Inhibitors. March 16, 2020. Available at: https://www.hemophilia.org/Researchers-Healthcare-Providers/Medical-and-Scientific-Advisory-Council-MASAC/MASAC-Recommendations/Recommendation-on-the-Use-and-Management-of-Emicizumab-kxwh-Hemlibra-for-Hemophilia-A-with-and-without-Inhibitors. Accessed on September 22, 2022.
9. Srivastava A, Santagostino E, Dougall A, et al. World Federation of Hemophilia. Guidelines for the management of hemophilia. Haemophilia. 3rd edition. August 2020. Available at https://onlinelibrary.wiley.com/doi/epdf/10.1111/hae.14046. Accessed on September 22, 2022.
10. Vonvendi – von Willebrand factor (recombinant) Package Insert. Baxalta US Inc. 2018. Available at file:///C:/Users/AF38863/Downloads/20190215_53b6d198-6175-4a26-8606-dc0d2a0f12d6%20(1).pdf Accessed on September 22, 2022.
11. Altuviiio – antihemophilic factor (recombinant), Fc-VWF-XTEN fusion protein-ehtl Package Insert. Bioverativ Therapeutics Inc. Available at https://www.fda.gov/media/165594/download. Accessed February 23, 2023.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.