Neighborhood Health Plan OF RHODE ISLAND™
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Hemophilia Products – Factor VIII/VWF Complex: Alphanate, Humate-P, Wilate
(Intravenous)

Effective date: 01/01/2020

Review date: 10/02/2019, 12/18/19, 1/22/20, 5/3/2021, 6/24/2021, 6/16/2022, 6/22/2023, 12/07/2023, 01/04/2024, 05/15/2024, 08/14/2024, 09/17/2025

Pharmacy Scope: Medicaid

Medical Scope: Medicaid, Commercial, Medicare

I. Length of Authorization

Unless otherwise specified*, the initial authorization will be provided for 3 months and may be renewed.

Note: The cumulative amount of medication the patient has on-hand will be taken into account for authorizations. Up to 5 'on-hand' doses for the treatment of acute bleeding episodes will be permitted at the time of the authorization request.

** Initial and renewal authorization periods may vary by specific covered indication*

II. Dosing Limits

A. Max Units (per dose and over time) [Medical Benefit]:

- Alphate: 55,200 billable units per 28 day supply
- Humate-P: 55,200 billable units per 28 day supply
- Wilate: 55,200 billable units per 90 day supply

III. Initial Approval Criteria

Hemophilia Management Program
Requirements for half-life study and inhibitor tests are a part of the hemophilia management program. This information is not meant to replace clinical decision making when initiating or modifying medication therapy and should only be used as a guide.

A. Alphanate, Humate-P ONLY

Coverage is provided in the following conditions:

- Medicare members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements.

Hemophilia A (congenital factor VIII deficiency) †

- Diagnosis of congenital factor VIII deficiency has been confirmed by blood coagulation testing; **AND**

- Will not be used in combination with another agent used as prophylactic therapy for Hemophilia A***see chart below; ADD
- Used as treatment in one of the following:
  - Treatment and control of acute bleeding episodes (episodic treatment of acute hemorrhage); **OR**
  - Perioperative management *(*Authorization is valid for 1 month)*; **OR**
  - Routine prophylaxis to prevent or reduce the frequency of bleeding episodes; **AND**
    - Used as primary prophylaxis in members with severe factor VIII deficiency (factor VIII level of <1%); **OR**
    - Used as secondary prophylaxis in members with at least TWO documented episodes of spontaneous bleeding into joints

Hemophilia Management Program
• If the request is for routine prophylaxis and the requested dose exceeds dosing limits under part II, a half-life study should be performed to determine the appropriate dose and dosing interval. • For members with a BMI ≥ 30, a half-life study should be performed to determine the appropriate dose and dosing interval. • For minimally treated members (< 50 exposure days to factor products) previously receiving a different factor product, inhibitor testing is required at baseline, then at every comprehensive care visit (yearly for the mild and moderate members, semi-annually for the severe members)

von Willebrand disease (vWD) † Φ

- Diagnosis of von Willebrand disease has been confirmed by blood coagulation and von Willebrand factor testing; **AND**
- Used as treatment in one of the following:
  - Spontaneous and trauma-induced bleeding episodes; **OR**
  - Surgical bleeding prophylaxis during major or minor procedures in members with vWD in whom desmopressin is either ineffective or contraindicated *(*Authorization valid for 1 month)* ; **AND**
- Alphanate is not indicated for members with severe (type 3) vWD undergoing major surgery OR treatment of spontaneous/trauma-induced bleeding episodes

Hemophilia Management Program
For minimally treated members (< 50 exposure days to factor products) previously receiving a different factor product, inhibitor testing is required at baseline, then at every comprehensive care visit (yearly for the mild and moderate members, semi-annually for the severe members)

B. **Wilate**

Hemophilia A (congenital factor VIII deficiency) †

- Diagnosis of congenital factor VIII deficiency has been confirmed by blood coagulation testing; **AND**
- Used as treatment in one of the following:
    - Control and prevention of bleeding episodes (episodic treatment of acute hemorrhage); **OR**
    - Routine prophylaxis to prevent or reduce the frequency of bleeding episodes; **AND**
        - Used as primary prophylaxis in members with severe factor VIII deficiency (factor VIII level of <1%); **OR**
        - Used as secondary prophylaxis in members with at least TWO documented episodes of spontaneous bleeding into joints

von Willebrand disease (vWD) † Φ

- Diagnosis of von Willebrand disease has been confirmed by blood coagulation and von Willebrand factor testing; **AND**
- Used as treatment in one of the following:
    - Perioperative management of bleeding *(*Authorization valid for 1 month)*; **OR**
    - On demand treatment and control of bleeding episodes in at least one of the following:
        - Members with severe vWD; **OR**
        - Members mild or moderate vWD in whom the use of desmopressin is known or suspected to be ineffective or contraindicated; **OR**
    - Routine prophylaxis to reduce the frequency of bleeding episodes;

***** Drugs to treat Hemophila A & B**

Hemophilia A & B Drug Chart	
Factor VIIa (Hemophilia A or B)	
Novoseven RT	J7189
Sevenfact	J7212
Anti-Inhibitor Coagulant Complex (Hemophilia A or B)	
Feiba	J7198
Factor VIII (Hemophilia A)	
Advate	J7192

Kogenate FS	J7192
Helixate FS	J7192
Recombinate	J7192
Kovaltry	J7211
Eloctate	J7205
Koate / Koate-DVI	J7190
Hemofil M	J7190
Novoeight	J7182
Nuwiq	J7209
Obizur	J7188
Xyntha / Xyntha Solofuse	J7185
Afstyla	J7210
Adynovate	J7207
Jivi	J7208
Esperoct	J7204
Altuviiio	J7214
Factor IX (Hemophilia B)	
AlphaNine SD	J7193
Mononine	J7193
Alprolix	J7201
Profilnine	J7194
BeneFIX	J7194
Ixinity	J7213

Rixubis	J7200
Idelvion	J7202
Rebinyn	J7203

Hemophilia Management Program
For minimally treated members (< 50 exposure days to factor products) previously receiving a different factor product, inhibitor testing is required at, then at every comprehensive care visit (yearly for the mild and moderate members, semi-annually for the severe members)

† FDA Approved Indication(s) **Φ** Orphan Drug

IV. Dispensing Requirements for Rendering Providers (Hemophilia Management Program)

- Prescriptions cannot be filled without an expressed need from the member, caregiver or prescribing practitioner. Auto-filling is not allowed.
- Monthly, rendering provider must submit for authorization of dispensing quantity before delivering factor product. Information submitted must include:
  - Original prescription information, requested amount to be dispensed, vial sizes available to be ordered from the manufacturer, and member clinical history (including member product inventory and bleed history)
  - Factor dose should not exceed +1% of the prescribed dose and a maximum of three vials may be dispensed per dose. If unable to provide factor dosing within the required threshold, below the required threshold, the lowest possible dose able to be achieved above +1% should be dispensed. Prescribed dose should not be increased to meet assay management requirements.
- The cumulative amount of medication(s) the member has on-hand should be taken into account when dispensing factor product. Members should not have more than 5 extra doses on-hand for the treatment of acute bleeding episodes.
- Dispensing requirements for renderings providers are a part of the hemophilia management program. This information is not meant to replace clinical decision making when initiating or modifying medication therapy and should only be used as a guide.

V. Renewal Criteria

Coverage can be renewed based upon the following criteria:

- Member continues to meet criteria identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: anaphylaxis and hypersensitivity reactions (e.g., angioedema, urticaria, tachycardia, chest tightness, hypotension, rash, nausea, vomiting, paresthesia, restlessness, wheezing, dyspnea, etc.), thromboembolic events (thromboembolism, pulmonary embolism), development of neutralizing antibodies (inhibitors), etc.; **AND**
- Any increases in dose must be supported by an acceptable clinical rationale (i.e. weight gain, half-life study results, increase in breakthrough bleeding when member is fully adherent to therapy, etc.); **AND**
- The cumulative amount of medication(s) the member has on-hand will be taken into account when authorizing. The authorization will allow up to 5 doses on-hand for the treatment of acute bleeding episodes as needed for the duration of the authorization; **AND**

Treatment and control of acute bleeding episodes/Treatment of Spontaneous and trauma-induced bleeding episodes/On-demand treatment of bleeding episodes

- Renewals will be approved for a 6 month authorization period

Perioperative management of surgical bleeding/Surgical bleeding prophylaxis

- Coverage may NOT be renewed

Routine prophylaxis to prevent or reduce the frequency of bleeding episode

- Renewals will be approved for a 12-month authorization period; **AND**
- Member has demonstrated a beneficial response to therapy (i.e., the frequency of bleeding episodes has decreased from pre-treatment baseline)

VI. Dosage/Administration

Alphanate

Indication	Dose
Control and prevention of bleeding Congenital Hemophilia A	The expected in vivo peak increase in FVIII level expressed as IU/dL (or % normal) can be estimated using the following formulas: Dosage (international units) = body weight (kg) x desired FVIII rise (IU/dL or % normal) x 0.5 (IU/kg per IU/dL) <u>Minor</u> FVIII:C levels should be brought to 30% of normal (15 IU FVIII/kg twice daily) until hemorrhage stops and healing has been achieved (1-2 days). <u>Moderate</u> FVIII:C levels should be brought to 50% of normal (25 IU FVIII/Kg twice daily). Treatment should continue until healing has been achieved (2-7 days, on average). <u>Major</u>

Indication	Dose
	FVIII:C levels should be brought to 80-100% of normal (40-50 IU FVIII/kg twice daily) for at least 3-5 days. Following this treatment period, FVIII levels should be maintained at 50% (25 IU FVIII/kg twice daily) until healing has been achieved. Major hemorrhages may require treatment for up to 10 days. Intracranial hemorrhages may require prophylaxis therapy for up to 6 months.
Perioperative management Congenital Hemophilia A	The expected in vivo peak increase in FVIII level expressed as IU/dL (or % normal) can be estimated using the following formulas: – *Dosage (international units) = body weight (kg) x desired FVIII rise (IU/dL or % normal) x 0.5 (IU/kg per IU/dL)* **OR** – *IU/dL (or % of normal) = [Total Dose (IU)/body weight (kg)] x 2* Prior to surgery, the levels of FVIII:C should be brought to 80-100% of normal (40-50 IU FVIII/kg). For the next 7-10 days, or until healing has been achieved, the member should be maintained at 60-100% of normal (30-50 IU FVIII/kg twice daily).
Control and prevention of bleeding and perioperative management von Willebrand Disease (VWD)	The ratio of VWF:RCo to FVIII in Alphanate varies by lot, so with each new lot, check the IU VWF:RCo/Vial to ensure accurate dosing. Minor *Pre-operative/pre-procedure dose (Target FVIII:C Activity – 40-50 IU/dL):* Adults: 60 IU VWF:RCo/kg body weight. Pediatrics: 75 IU VWF:RCo/kg body weight. *Maintenance dose (Target FVIII:C Activity – 40-50 IU/dL):* Adults: 40- 60 IU VWF:RCo/kg body weight at 8 to 12 hour intervals as clinically needed for 1-3 days. Pediatrics: 50-75 IU VWF:RCo/kg body weight at 8 to 12 hour intervals as clinically needed for 1-3 days. Major *Pre-operative/pre-procedure dose (Target FVIII:C Activity – 100 IU/dL):* Adults: 60 IU VWF:RCo/kg body weight. Pediatrics: 75 IU VWF:RCo/kg body weight. *Maintenance dose (Target FVIII:C Activity – 100 IU/dL):* Adults: 40-60 IU VWF:RCo/kg body weight at 8 to 12 hour intervals as clinically needed for at least 3-7 days. Pediatrics: 50- 75 IU VWF:RCo/kg body weight at 8 to 12 hour intervals as clinically needed for at least 3-7 days.

Humate-P

Indication	Dose
Control and prevention of bleeding Congenital Hemophilia A	One International Unit (IU) of Factor VIII (FVIII) activity per kg body weight will increase the circulating FVIII level by approximately 2.0 International Units (IU)/dL. Minor

Indication	Dose
	Loading Dose: Adminster 15 IU FVIII:C/kg intravenously to achieve a FVIII:C plasma level of approximately 30% of normal; one infusion may be sufficient. If needed, half of the loading dose may be given once or twice daily for 1-2 days. Moderate Loading Dose: Adminster 25 IU FVIII:C/kg intravenously to achieve a FVIII:C plasma level of approximately 50% of normal, followed by 15 IU FVIII:C/kg every 8-12 hours for the first 1-2 days to maintain the FVIII:C plasma level at 30% of normal. Continue the same dose once or twice daily for up to 7 days or until adequate wound healing is achieved. Major Initially adminster 40-50 IU FVIII:C/kg intravenously, followed by 20-25 IU FVIII:C/kg every 8 hours to maintain the FVIII:C plasma level at 80-100% of normal for 7 days. Continue the same dose once or twice daily for another 7 days to maintain the FVIII:C level at 30-50% of normal.
Control and prevention of bleeding von Willebrand Disease (VWD)	Administer 40-80 IU VWF:RCo intravenously (corresponding to 17-33 IU FVIII in Humate-P) per kg body weight every 8 to 12 hours. Adjust the dosage based on the extent and location of bleeding. Administer repeat doses as long as needed based on monitoring of appropriate clinical and laboratory measures
Perioperative management von Willebrand Disease (VWD)	**Loading Doses** ***(to be administered 1 to 2 hours before surgery)*** Major *VWF:RCo Target Peak Plasma Level: 100 IU/dL* *FVIII:C Target Peak Plasma Level: 80-100 IU/dL* *Calculation of Loading Dose:* ((Target peak plasma VWF:RCo level – baseline plasma VWF:RCo level) –Body wt (kg)) /IVR (in vivo recovery) If the IVR is not available, assume an IVR of 2.0 IU/dL per IU/kg and calculate the loading dose as follows: (100 – baseline plasma VWF:RCo) x Body Weight (kg)/2.0 Minor *VWF:RCo Target Peak Plasma Level: 50-60 IU/dL* *FVIII:C Target Peak Plasma Level: 40-50 IU/dL* *Calculation of Loading Dose:* (Target peak plasma VWF:RCo level – baseline plasma VWF:RCo level) –Body weight (kg)) /IVR (in vivo recovery) Emergency *VWF:RCo Target Peak Plasma Level: 100 IU/dL* *FVIII:C Target Peak Plasma Level: 80-100 IU/dL* Administer a dose of 50-60 IU VWF:RCo/kg body weight. **Maintenance Doses** The initial maintenance dose of Humate-P for the prevention of excessive bleeding during and after surgery should be half of the loading dose, irrespective of additional dosing required to meet FVIII:C targets. Subsequent maintenance doses should be based on the member's VWF:RCo and FVIII levels.

Wilate

Indication	Dose
Control of bleeding episodes von Willebrand Disease (VWD)	Calculation of the required dose of VWF:RCo is based on the empirical finding that 1 IU VWF:RCo per kg body weight raises the plasma VWF activity by approximately 2% of normal activity or 2 IU/dL, using the following formula: – *Required IU = body weight (kg) x desired VWF;RCo rise (%) (IU/dL) x 0.5 (IU/kg per IU/dL)* – *Expected VWF:RCo rise (% of normal) = 2 x administered IU / body weight (kg)* Adjust the dosage and frequency of administration to the clinical effectiveness in the individual member. The ratio between VWF:RCo and FVIII activities in Wilate is approximately 1:1. The dosage should be adjusted according to the extent and location of the bleeding. Minor Loading Dose: Administer 20-40 IU/kg intravenously Maintenance Dose: Adminster 20-30 IU/kg intravenously every 12-24 hours, as needed for up to 3 days VWF:RCo and FVIII activity trough levels > 30%. Major Loading Dose: Administer 40-60 IU/kg intravenously Maintenance Dose: Administer 20-40 IU/kg intravenously every 12-24 hours as needed for up to 5-7 days VWF:RCo and FVIII activity trough levels > 50%.
Perioperative management of bleeding von Willebrand Disease (vWD)	Calculation of the required dose of VWF:RCo is based on the empirical finding that 1 IU VWF:RCo per kg body weight raises the plasma VWF activity by approximately 2% of normal activity or 2 IU/dL, using the following formula: – *Required IU = body weight (kg) x desired VWF;RCo rise (%) (IU/dL) x 0.5 (IU/kg per IU/dL)* – *Expected VWF:RCo rise (% of normal) = 2 x administered IU / body weight (kg)* Adjust the dosage and frequency of administration to the clinical effectiveness in the individual member. Minor Loading Dose: Administer 30-60 IU/kg intravenously Maintenance dose: Administer 15-30 IU/kg intravenously or half of the loading dose every every 12-24 hours until wound healing achieved, up to 3 days. VWF:RCo trough levels > 30% and peak levels 50%. Major Loading dose: Adminster 40-60 IU/kg intravenously Maintenance dose: Administer 20-40 IU/kg intravenously or half the loading dose every 12-24 hours (at least 2 doses within the first 24 hours after the start of surgery) until wound healing achieved, up to 6 days or more. VWF:RCo trough levels > 50% and peak levels 100%.
Routine Prophylaxis von Willebrand Disease (VWD)	Calculation of the required dose of VWF:RCo is based on the empirical finding that 1 IU VWF:RCo per kg body weight raises the plasma VWF activity by approximately 2% of normal activity or 2 IU/dL, using the following formula: – *Required IU = body weight (kg) x desired VWF:RCo rise (%) (IU/dL) x 0.5 (IU/kg per IU/dL)*

<table>
<tr><th>Indication</th><th>Dose</th></tr>
<tr><td></td><td>– Expected VWF:RCo rise (% of normal) = 2 x administered IU / body weight (kg)
Adjust the dosage and frequency of administration to the clinical effectiveness in the individual member.
<u>Adults and pediatric members at least 6 years of age:</u> Administer 20-40 IU/kg intravenously 2 or 3 times per week</td></tr>
<tr><td>Control and prevention of bleeding/ Routine Prophylaxis Congenital Hemophilia A</td><td>Calculation of the required dose of Factor VIII is based on the empirical finding that 1 IU Factor VIII per kg body weight raises the plasma Factor VIII activity by approximately 2% of normal activity or 2 IU/dL when assessed using the one stage clotting assay. Use the following formula to determine the required dose:
– Required IU = body weight (kg) x desired Factor VIII rise (%) (IU/dL) x 0.5 (IU/kg per IU/dL)
– Expected Factor VIII rise (% of normal) = 2 x administered IU / body weight (kg)
Dose and duration of therapy depend on the member's weight, type and severity of hemorrhage, FVIII level, and presence of inhibitors. Titrate dose and frequency to the member's clinical response, individual needs, severity of deficiency, severity of hemorrhage, desired FVIII level, and presence of inhibitor, and the member's clinical condition. Members may vary in their pharmacokinetic (e.g., half-life, in vivo recovery) and clinical responses to Wilate.
<u>Routine Prophylaxis</u>
A guide for dosing as routine prophylaxis to reduce the frequency of bleeding is provided below. Exact dosing should be defined by the member's clinical status and response.
<table>
<tr><th>Members</th><th>Recommended Dose (IU/kg)</th><th>Frequency</th></tr>
<tr><td>Adolescents and adults</td><td>20-40 IU/kg</td><td>Every 2-3 days</td></tr>
</table>
<u>Treatment of Hemorrhages</u>
A guide for dosing in the treatment of major and minor hemorrhages is provided below. Exact dosing should be defined by the member's clinical status and response.
<table>
<tr><th>Hemorrhage Type</th><th>Recommended Dose (IU/kg)</th><th>Frequency</th><th>Frequency</th></tr>
<tr><td>Minor</td><td>30-40</td><td>Repeat every 12-24 hours</td><td>At least 1 day, until bleed stops</td></tr>
<tr><td>Moderate</td><td>30-40</td><td>Repeat every 12-24 hours</td><td>3+ days, until bleed stops</td></tr>
<tr><td>Major</td><td>35-50</td><td>Repeat every 12-24 hours</td><td>3+ days, until bleed stops</td></tr>
<tr><td>Life-Threatening</td><td>35-50</td><td>Repeat every 8-24 hours</td><td>Until threat has resolved</td></tr>
</table></td></tr>
</table>

VII. Summary of Evidence

Alphanate is an Antihemophilic Factor/von Willebrand Factor Complex (Human) indicated for control and prevention of bleeding in patients with hemophilia A or acquired Factor VIII (FVIII) deficiency, surgical and/or invasive procedures in adult and pediatric patients with von Willebrand Disease in whom desmopressin (DDAVP) is either ineffective or contraindicated. In a prospective, multi-center clinical study, 37 subjects with VWD underwent 59 surgical procedures. The surgeries were categorized as major, minor or invasive procedures according to definitions used in the study. The outcome of each surgery was evaluated according to a clinical rating scale (excellent, good, poor or none) and was considered successful if the outcome was excellent or good (primary endpoint). The effect of treatment on surgical prophylaxis analysis per treated event with Alphanate (A-SD/HT) had an absolute frequency & proportion of successful outcomes of 22/24 (91.66%) and a 95% Confidence Interval (CI) for the proportion of subjects with successful prophylaxis (0.7300 to 0.9897). A retrospective, multi-center study was performed to assess the efficacy of Alphanate (ASD/HT) as replacement therapy in preventing excessive bleeding in subjects with congenital VWD undergoing surgical or invasive procedures, for whom DDAVP® was ineffective or inadequate. The primary efficacy variable was the overall treatment outcome for each surgical or invasive procedure, as rated by the investigator using a 4-point verbal

rating scale (VRS): "excellent," "good," "poor," or "none (no indication of efficacy)." The categorization of the replacement treatment outcome according to the proposed scale was based upon the investigator's clinical experience and an independent referee committee. More than 90% received an investigator and referee's overall and daily rating of "effective" ("excellent" or "good") with a p value of < 0.0001. The majority of ratings were "excellent" (≥ 81.3% in each VWD type). The most frequent adverse events reported with Alphanate in > 5% of patients are respiratory distress, pruritus, rash, urticaria, face edema, paresthesia, pain, fever, chills, joint pain and fatigue.

Humate-P is an Antihemophilic Factor/von Willebrand Factor (VWF) Complex (Human) indicated for Hemophilia A – treatment and prevention of bleeding in adults and Von Willebrand disease (VWD) – in adults and pediatric patients in the treatment of spontaneous and trauma-induced bleeding episodes, and prevention of excessive bleeding during and after surgery. Clinical efficacy of Humate-P in the control of bleeding in subjects with VWD was determined by a retrospective review of clinical safety and efficacy data obtained from 97 Canadian VWD subjects who received product under an Emergency Drug Release Program. Humate-P was administered to 97 subjects in 530 treatment courses: 73 for surgery, 344 for treatment of bleeding, and 20 for prophylaxis of bleeding. Two prospective, open-label, non-controlled, multicenter clinical studies, one in the US and one in Europe, investigated the safety and hemostatic efficacy of Humate-P in subjects with VWD undergoing surgery. The primary endpoint was the investigator's end-of-surgery hemostatic efficacy assessment. The investigator's end-of-surgery hemostatic efficacy assessment for the US study had a 95% confidence interval (CI) for effective proportion of 78.5-97.6%. The investigator's overall hemostatic efficacy assessment for the US study had a 95% CI for effective proportion of 91.3-100%. In the US study, all efficacy assessments were reviewed by an independent Data Safety Monitoring Board (DSMB). The DSMB agreed with the investigators' assessments of the overall hemostatic efficacy for all but two subjects (neither of whom had type 3 VWD). Based on this, the DSMB judged hemostatic efficacy as "effective" in 33 (94.3%) (95% CI: 81.1% to 99.0%) of the 35 subjects. The most common adverse reactions observed by >5% of subjects after receiving Humate-P are allergic-anaphylactic reactions (e.g., urticaria, chest tightness, rash, pruritus, edema) and, in patients undergoing surgery, postoperative wound and injection-site bleeding, and epistaxis.

Wilate is indicated in children and adults with von Willebrand disease for on-demand treatment and control of bleeding episodes, perioperative management of bleeding, and routine prophylaxis to reduce the frequency of bleeding episodes. Wilate is indicated for routine prophylaxis in children 6 years of age and older and adults with von Willebrand disease. Clinical efficacy of Wilate in the control of bleeding in subjects with VWD was determined in four prospective, open-label, non-controlled clinical studies (excluding PK study). In assessing efficacy using the objective criteria, treatment of a bleeding episode was classified as a success when none of the criteria listed below were met: the episode was additionally treated with another VWF-containing product (excluding whole blood), the subject received a blood transfusion during the episode, follow-up treatment with a daily dosage of WILATE that was greater than or equal to 50% (≥ 50%) above the initial dose (for bleeding episodes with more than 1 day of treatment), treatment duration of more than 4 days (> 4 days) in cases of severe bleeding (other than gastrointestinal), treatment duration of more than 3 days (> 3 days) in cases of moderate bleeding (other than gastrointestinal), treatment duration of more than 2 days (> 2 days) in cases of minor bleeding (other than gastrointestinal), or the last efficacy rating of the bleeding episode was "moderate" or "none". Using the above objective criteria, corresponding efficacy for each bleeding event was rated as being successful in 84% of the episodes. The majority of BEs were treated for 1-3 days. In subjects with GI bleeds, the duration for product use to control bleeding was longer (up to 7 days). A prospective, open-label, single-arm, uncontrolled, multi-center clinical study was conducted to investigate the safety and hemostatic efficacy of Wilate

in 28 subjects who underwent 30 surgeries. Efficacy of Wilate in surgical procedures was assessed by the surgeon at the conclusion of surgery and by the investigator-hematologist at 24 hours following completion of the final maintenance dose. Efficacy of Wilate was assessed using a stringent and objective 4-point ordinal efficacy scale (excellent, good, moderate, or none) based on estimated expected versus actual blood loss, transfusion requirements and post-operative bleeding and oozing. The primary end point was a rating of excellent or good to declare the outcome a success. The overall efficacy of Wilate treatment for surgical procedures in this study was 96.7%. Treatment with Wilate was successful in all minor surgeries and in 95.2% of major surgeries (98.75% CI: 0.784, 1.000). It was also successful in all surgical procedures in VWD type 3 and type 2 subjects and in 85.7% of procedures in VWD type 1 subjects (98.75% CI: 0.785, 1.000). The most common adverse reactions (≥ 1%) in clinical trials on VWD were hypersensitivity reactions, urticaria, chest discomfort, and dizziness. The most common adverse reaction (≥ 1%) in clinical trials in hemophilia A was pyrexia (fever).

VIII. Billing Code/Availability Information

HCPCS Code (s)& NDC(s):

Drug	Manufacturer	J-Code	1 Billable Unit Equiv.	Vial Size	NDC
Alphanate	Grifols Biologicals, LLC	J7186	1 IU	250 units	- 68516-4601 - 68516-4611
				500 units	- 68516-4602 - 68516-4612
				1000 units	- 68516-4603 - 68516-4613
				1500 units	- 68516-4604 - 68516-4614
				2000 units	- 68516-4609 - 68516-4615
Humate-P	CSL Behring LLC	J7187	1 IU	600 units	63833-0615
				1200 units	63833-0616
				2400 units	63833-0617
Wilate	Octapharma USA, Inc	J7183	1 IU VWF:RCO	500 units	67467-0182
				1000 units	

IX. References

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14. Palmetto GBA. Local Coverage Article: Billing and Coding: Guidance for Anti-Inhibitor Coagulant Complex (AICC) National Coverage Determination (NCD) 110.3 (A56065). Centers for Medicare & Medicaid Services Inc. Updated on 11/14/2022 with effective date 11/24/2022. Accessed May 2024.
15. Novitas Solutions, Inc. Local Coverage Article: Billing and Coding: Hemophilia Factor Products (A56433). Centers for Medicare & Medicaid Services Inc. Updated on 09/29/2023 with effective date 10/01/2023. Accessed May 2024.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D66	Hereditary factor VIII deficiency
D68.01	Von Willebrand disease, type 1

ICD-10	ICD-10 Description
D68.020	Von Willebrand disease, type 2A
D68.021	Von Willebrand disease, type 2B
D68.022	Von Willebrand disease, type 2M
D68.023	Von Willebrand disease, type 2N
D68.03	Von Willebrand disease, type 3
D68.04	Acquired von Willebrand disease
D68.09	Other von Willebrand disease

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes		
Jurisdiction	**NCD/LCA/LCD Document (s)**	**Contractor**
N	A56482	First Coast Service Options, Inc.
J, M	A56065	Palmetto GBA
H,L	A56433	Novitas Solutions, Inc.

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Policy Rationale: Humate, Alphanate, and Wilate were reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Humate, Alphanate, and Wilate according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For Medicare members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.