

## 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

Scope: Medicaid, Commercial, Medicare-Medicaid Plan (MMP)

### 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. Quantity Limit (max daily dose) [Pharmacy Benefit]:

N/A

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

- Alphanate: 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:

#### 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:
    - 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 patients with severe factor VIII deficiency (factor VIII level of <1%); **OR**
  - Used as secondary prophylaxis in patients 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  $\geq 30$ , a half-life study should be performed to determine the appropriate dose and dosing interval.
- For minimally treated patients (< 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 patients, semi-annually for the severe patients)

#### 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 patients with vWD in whom desmopressin is either ineffective or contraindicated (*\*Authorization valid for 1 month*); **AND**
- Alphanate is not indicated for patients with severe (type 3) vWD undergoing major surgery OR treatment of spontaneous/trauma-induced bleeding episodes

#### Hemophilia Management Program

For minimally treated patients (< 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 patients, semi-annually for the severe patients)

#### 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 patients with severe factor VIII deficiency (factor VIII level of <1%); **OR**
  - Used as secondary prophylaxis in patients 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:
    - Patients with severe vWD; **OR**
    - Patients 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;

**Hemophilia Management Program**

For minimally treated patients (< 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 patients, semi-annually for the severe patients)

† 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 patient, 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 patient clinical history (including patient 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 patient has on-hand should be taken into account when dispensing factor product. Patients 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:

- Patient 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 patient is fully adherent to therapy, etc.); **AND**
- The cumulative amount of medication(s) the patient 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**
- Patient 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	<p>The expected in vivo peak increase in FVIII level expressed as IU/dL (or % normal) can be estimated using the following formulas:</p> <p>Dosage (international units) = body weight (kg) x desired FVIII rise (IU/dL or % normal) x 0.5 (IU/kg per IU/dL)</p> <p><u>Minor</u></p> <p>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).</p> <p><u>Moderate</u></p> <p>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).</p> <p><u>Major</u></p> <p>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.</p>
Perioperative management Congenital Hemophilia A	<p>The expected in vivo peak increase in FVIII level expressed as IU/dL (or % normal) can be estimated using the following formulas:</p> <ul style="list-style-type: none"> <li>– <i>Dosage (international units) = body weight (kg) x desired FVIII rise (IU/dL or % normal) x 0.5 (IU/kg per IU/dL)</i> <b>OR</b></li> <li>– <i>IU/dL (or % of normal) = [Total Dose (IU)/body weight (kg)] x 2</i></li> </ul> <p>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 patient should be maintained at 60-100% of normal (30-50 IU FVIII/kg twice daily).</p>
Control and prevention of bleeding and perioperative management von Willebrand Disease (VWD)	<p>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.</p> <p><u>Minor</u></p> <p><u>Pre-operative/pre-procedure dose (Target FVIII:C Activity – 40-50 IU/dL):</u></p> <p>Adults: 60 IU VWF:RCo/kg body weight.</p> <p>Pediatrics: 75 IU VWF:RCo/kg body weight.</p> <p><u>Maintenance dose (Target FVIII:C Activity – 40-50 IU/dL):</u></p> <p>Adults: 40- 60 IU VWF:RCo/kg body weight at 8 to 12 hour intervals as clinically needed for 1-3 days.</p> <p>Pediatrics: 50-75 IU VWF:RCo/kg body weight at 8 to 12 hour intervals as clinically needed for 1-3 days.</p> <p><u>Major</u></p> <p><u>Pre-operative/pre-procedure dose (Target FVIII:C Activity – 100 IU/dL):</u></p>

Indication	Dose
	<p>Adults: 60 IU VWF:RCo/kg body weight.            Pediatrics: 75 IU VWF:RCo/kg body weight.  <u>Maintenance dose (Target FVIII:C Activity – 100 IU/dL):</u>            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.</p>

### Humate-P

Indication	Dose
Control and prevention of bleeding Congenital Hemophilia A	<p>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.</p> <p><u>Minor</u>  <u>Loading Dose:</u> 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.</p> <p><u>Moderate</u>  <u>Loading Dose:</u> 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.</p> <p><u>Major</u>            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.</p>
Control and prevention of bleeding von Willebrand Disease (VWD)	<p>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</p>
Perioperative management von Willebrand Disease (VWD)	<p><b><u>Loading Doses (to be administered 1 to 2 hours before surgery)</u></b></p> <p><u>Major</u>  <u>VWF:RCo Target Peak Plasma Level: 100 IU/dL</u>  <u>FVIII:C Target Peak Plasma Level: 80-100 IU/dL</u>  <u>Calculation of Loading Dose:</u>            ((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</p> <p><u>Minor</u>  <u>VWF:RCo Target Peak Plasma Level: 50-60 IU/dL</u></p>



Indication	Dose
	<p><u>FVIII:C Target Peak Plasma Level: 40-50 IU/dL</u></p> <p><u>Calculation of Loading Dose:</u> ((Target peak plasma VWF:RCo level – baseline plasma VWF:RCo level) – Body weight (kg)) /IVR (in vivo recovery)</p> <p><u>Emergency</u></p> <p><u>VWF:RCo Target Peak Plasma Level: 100 IU/dL</u></p> <p><u>FVIII:C Target Peak Plasma Level: 80-100 IU/dL</u></p> <p>Administer a dose of 50-60 IU VWF:RCo/kg body weight.</p> <p><b><u>Maintenance Doses</u></b></p> <p>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 patient’s VWF:RCo and FVIII levels.</p>

**Wilate**

Indication	Dose
<p>Control of bleeding episodes von Willebrand Disease (VWD)</p>	<p>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:</p> <ul style="list-style-type: none"> <li>- <i>Required IU = body weight (kg) × desired VWF:RCo rise (%) (IU/dL) × 0.5 (IU/kg per IU/dL)</i></li> <li>- <i>Expected VWF:RCo rise (% of normal) = 2 × administered IU / body weight (kg)</i></li> </ul> <p>Adjust the dosage and frequency of administration to the clinical effectiveness in the individual patient.</p> <p>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.</p> <p><b><u>Minor</u></b></p> <p><b><u>Loading Dose:</u></b> Administer 20-40 IU/kg intravenously</p> <p><b><u>Maintenance Dose:</u></b> Administer 20-30 IU/kg intravenously every 12-24 hours, as needed for up to 3 days VWF:RCo and FVIII activity trough levels &gt; 30%.</p> <p><b><u>Major</u></b></p> <p><b><u>Loading Dose:</u></b> Administer 40-60 IU/kg intravenously</p> <p><b><u>Maintenance Dose:</u></b> 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 &gt; 50%.</p>
<p>Perioperative management of bleeding von Willebrand Disease (vWD)</p>	<p>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:</p> <ul style="list-style-type: none"> <li>- <i>Required IU = body weight (kg) × desired VWF:RCo rise (%) (IU/dL) × 0.5 (IU/kg per IU/dL)</i></li> <li>- <i>Expected VWF:RCo rise (% of normal) = 2 × administered IU / body weight (kg)</i></li> </ul> <p>Adjust the dosage and frequency of administration to the clinical effectiveness in the individual patient.</p> <p><b><u>Minor</u></b></p>

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	<p><u>Loading Dose:</u> Administer 30-60 IU/kg intravenously</p> <p><u>Maintenance dose:</u> Administer 15-30 IU/kg intravenously or half of the loading dose every 12-24 hours until wound healing achieved, up to 3 days. VWF:RCo trough levels &gt; 30% and peak levels 50%.</p> <p><u>Major</u></p> <p><u>Loading dose:</u> Administer 40-60 IU/kg intravenously</p> <p><u>Maintenance dose:</u> 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 &gt; 50% and peak levels 100%.</p>																										
<p>Routine Prophylaxis von Willebrand Disease (VWD)</p>	<p>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:</p> <ul style="list-style-type: none"> <li>- <math>Required\ IU = body\ weight\ (kg) \times desired\ VWF:RCo\ rise\ (\%) \ (IU/dL) \times 0.5\ (IU/kg\ per\ IU/dL)</math></li> <li>- <math>Expected\ VWF:RCo\ rise\ (\% \ of\ normal) = 2 \times administered\ IU / body\ weight\ (kg)</math></li> </ul> <p>Adjust the dosage and frequency of administration to the clinical effectiveness in the individual patient.</p> <p><u>Adults and pediatric patients at least 6 years of age:</u> Administer 20-40 IU/kg intravenously 2 or 3 times per week</p>																										
<p>Control and prevention of bleeding/ Routine Prophylaxis Congenital Hemophilia A</p>	<p>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:</p> <ul style="list-style-type: none"> <li>- <math>Required\ IU = body\ weight\ (kg) \times desired\ Factor\ VIII\ rise\ (\%) \ (IU/dL) \times 0.5\ (IU/kg\ per\ IU/dL)</math></li> <li>- <math>Expected\ Factor\ VIII\ rise\ (\% \ of\ normal) = 2 \times administered\ IU / body\ weight\ (kg)</math></li> </ul> <p>Dose and duration of therapy depend on the patient's weight, type and severity of hemorrhage, FVIII level, and presence of inhibitors. Titrate dose and frequency to the patient's clinical response, individual needs, severity of deficiency, severity of hemorrhage, desired FVIII level, and presence of inhibitor, and the patient's clinical condition. Patients may vary in their pharmacokinetic (e.g., half-life, in vivo recovery) and clinical responses to Wilate.</p> <p><b><u>Routine Prophylaxis</u></b></p> <p>A guide for dosing as routine prophylaxis to reduce the frequency of bleeding is provided below. Exact dosing should be defined by the patient's clinical status and response.</p> <table border="1" data-bbox="613 1486 1351 1543"> <thead> <tr> <th>Patients</th> <th>Recommended Dose (IU/kg)</th> <th>Frequency</th> </tr> </thead> <tbody> <tr> <td>Adolescents and adults</td> <td>20-40 IU/kg</td> <td>Every 2-3 days</td> </tr> </tbody> </table> <p><b><u>Treatment of Hemorrhages</u></b></p> <p>A guide for dosing in the treatment of major and minor hemorrhages is provided below. Exact dosing should be defined by the patient's clinical status and response.</p> <table border="1" data-bbox="500 1661 1463 1808"> <thead> <tr> <th>Hemorrhage Type</th> <th>Recommended Dose (IU/kg)</th> <th>Frequency</th> <th>Frequency</th> </tr> </thead> <tbody> <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> </tbody> </table>	Patients	Recommended Dose (IU/kg)	Frequency	Adolescents and adults	20-40 IU/kg	Every 2-3 days	Hemorrhage Type	Recommended Dose (IU/kg)	Frequency	Frequency	Minor	30-40	Repeat every 12-24 hours	At least 1 day, until bleed stops	Moderate	30-40	Repeat every 12-24 hours	3+ days, until bleed stops	Major	35-50	Repeat every 12-24 hours	3+ days, until bleed stops	Life-Threatening	35-50	Repeat every 8-24 hours	Until threat has resolved
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## VII. 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	

## VIII. References

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4. MASAC Recommendations Concerning Products Licensed For The Treatment Of Hemophilia And Selected Disorders of the Coagulation System. Revised April 11, 2024. National Hemophilia Foundation. MASAC Document #284; April 2024. Available at: <http://www.bleeding.org/>. Accessed May 2024.
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## Appendix 1 – Covered Diagnosis Codes

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