Clinical Policy: Factor VIII/von Willebrand Factor Complex (Human - Alphanate, Humate-P, Wilate)
Reference Number: ERX.SPA.185
Effective Date: 01.11.17
Last Review Date: 11.17

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
The following are factor VIII/von Willebrand factor complexes (human) requiring prior authorization: Alphanate®, Humate®-P, and Wilate®.

FDA Approved Indication(s)
Alphanate is indicated:
- For control and prevention of bleeding episodes and perioperative management in adult and pediatric patients with Factor VIII deficiency due to hemophilia A
- For surgical and/or invasive procedures in adult and pediatric patients with von Willebrand Disease (VWD) in whom desmopressin (DDAVP) is either ineffective or contraindicated

Limitation(s) of use: Alphanate is not indicated for patients with severe VWD (Type 3) undergoing major surgery.

Humate-P is indicated:
- For treatment and prevention of bleeding in adults with hemophilia A (classical hemophilia)
- In adult and pediatric patients with VWD for:
  - Treatment of spontaneous and trauma-induced bleeding episodes, and
  - Prevention of excessive bleeding during and after surgery. This applies to patients with severe VWD as well as patients with mild to moderate VWD where use of DDAVP is known or suspected to be inadequate

Wilate is indicated in children and adults with VWD for:
- On-demand treatment and control of bleeding episodes
- Perioperative management of bleeding

Limitation(s) of use: Wilate is not indicated for the treatment of hemophilia A.

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Alphanate, Humate-P, and Wilate are medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Hemophilia A (must meet all):
      1. Diagnosis of hemophilia A, and request is for one of the following (a or b):
         a. Treatment and/or prevention of bleeding, and (i and ii):
            i. Request is for Alphanate or Humate-P;
            ii. If request is for Humate-P, age ≥ 18 years;
         b. Perioperative management, and
            i. Request is for Alphanate;
3. If factor VIII coagulant activity levels are > 5%, member has failed a trial of desmopressin acetate, unless contraindicated or clinically significant adverse effects are experienced, or an appropriate formulation of desmopressin acetate is not available;
4. Dose does not exceed the FDA approved maximum recommended dose for the relevant indications.

Approval duration: 3 months

B. **Von Willebrand Disease** (must meet all):
   1. Diagnosis of VWD (types 1, 2, or 3);
      a. For VWD types 1 and 2, member has failed a trial of desmopressin acetate, unless contraindicated or clinically significant adverse effects are experienced;
   2. Request is for one of the following (a or b):
      a. For spontaneous and trauma-induced bleeding episodes (Humate-P and Wilate only);
      b. Perioperative management;
         i. For Alphanate requests: if VWD type 3, documentation that the member is NOT undergoing major surgery;
   3. Prescribed by or in consultation with a hematologist;
   4. Dose does not exceed the FDA approved maximum recommended dose for the relevant indications.

Approval duration: 3 months

C. **Other diagnoses/indications**
   1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. **Continued Therapy**
A. **All Indications in Section I** (must meet all):
   1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria.
   2. If request is for a dose increase, new dose does not exceed the FDA approved maximum recommended dose for the relevant indications.

Approval duration: 3 months

B. **Other diagnoses/indications** (must meet 1 or 2):
   1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.

Approval duration: Duration of request or 3 months (whichever is less); or
   2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. **Diagnoses/Indications for which coverage is NOT authorized:**
   A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. **Appendices/General Information**
   **Appendix A: Abbreviation/Acronym Key**
   DDAVP: desmopressin acetate
   FDA: Food and Drug Administration
   VWD: von Willebrand disease

   **Appendix B: Therapeutic Alternatives**
### Drug Name
Desmopressin acetate

#### Dosing Regimen
- **Injection:** 0.3 mcg/kg IV every 48 hours
- **Nasal spray:**
  - < 50 kg: 1 spray intranasally in one nostril only; may repeat based on laboratory response and clinical condition
  - ≥ 50 kg: 1 spray intranasally in each nostril; may repeat based on laboratory response and clinical condition

#### Dose Limit/Maximum Dose
- Injection: 0.3 mcg/kg IV every 48 hours
- Nasal spray: 1 spray intranasally in each nostril

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**Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.**

### V. Dosage and Administration

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
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</thead>
</table>
| Factor VIII/von Willebrand factor complex (Alphanate) | Hemophilia A - control and prevention of bleeding episodes | Minor episodes: 15 IU/kg IV every 12 hours
Moderate episodes: 25 IU/kg IV every 12 hours
Major episodes: 40-50 IU/kg IV initially followed by 25 IU/kg IV every 8-12 hours | 100 IU/kg/day |
| Factor VIII/von Willebrand factor complex (Humate-P) | Hemophilia A - control and prevention of bleeding episodes | Minor episodes: 15 IU/kg IV loading dose followed by half of the loading dose given once or twice daily if needed
Moderate episodes: 25 IU/kg IV loading dose followed by 15 IU/kg IV every 8-12 hours
Major episodes: 40-50 IU/kg IV initially followed by 20-25 IU/kg IV every 8 hours | 75 IU/kg/day |
| Factor VIII/von Willebrand factor complex (Alphanate) | Hemophilia A – perioperative management | Pre-operative: 40-50 IU/kg IV once as a single dose
Post-operative: 30-50 IU/kg IV every 12 hours | 100 IU/kg/day |
| Factor VIII/von Willebrand factor complex (Humate-P) | VWD – control and prevention of bleeding episodes | Type 1 VWD, mild disease
Minor or major episodes: 40-60 IU/kg | 240 IU/kg/day |
<table>
<thead>
<tr>
<th>Drug Name</th>
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<th>Maximum Dose</th>
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| Factor VIII/von Willebrand factor complex (Wilate) | VWD – control and prevention of bleeding episodes    | All VWD types  
Type 1 VWD, moderate or severe disease  
Minor episodes: 40-50 IU/kg IV as one or two doses  
Major episodes: 50-75 IU/kg loading dose followed by 40-60 IU/kg every 8-12 hours  
Type 2 or 3 VWD  
Minor episodes: 40-50 IU/kg IV as one or two doses  
Major episodes: 60-80 IU/kg IV loading dose followed by 40-60 IU/kg every 8-12 hours | 80 IU/kg/day |
| Factor VIII/von Willebrand factor complex (Alphanate) | VWD – perioperative management (except Type 3 patients undergoing major surgery) | Pre-operative: (adults)  
60 IU/kg IV once as a single dose; (pediatrics)  
75 IU/kg IV once as a single dose  
Maintenance: (adults)  
40-60 IU/kg IV every 8-12 hours; (pediatrics)  
50-75 IU/kg IV every 8-12 hours | 225 IU/kg/day |
| Factor VIII/von Willebrand factor complex (Humate-P) | VWD – perioperative management                      | Minor or major surgery:  
IU required = (Plasma VWF:RCo_{time=30 min} – Plasma VWF:RCo_{baseline}) x body weight (kg) / IVR  
For major surgeries, if the IVR is not available, assume an IVR of 2.0 | Varies |
Factor VIII/von Willebrand factor complex (Wilate)

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
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</thead>
<tbody>
<tr>
<td>Factor VIII/von Willebrand factor complex (Wilate)</td>
<td>VWD – perioperative management</td>
<td>IU/dL per IU/kg and calculate the loading dose as follows: (100 – baseline plasma VWF:RCo) x body weight(kg) / 2.0</td>
<td>80 IU/kg/day</td>
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</tbody>
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Emergency surgery: 50-60 IU/kg IV one time

Minor surgery: 30-60 IU/kg IV loading dose followed by 15-30 IU/kg IV every 12-24 hours

Major surgery: 40-60 IU/kg IV loading dose followed by 20-40 IU/kg or half the loading dose every 12-24 hours

VI. Product Availability

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Availability</th>
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<tbody>
<tr>
<td>Factor VIII/von Willebrand factor complex (Alphanate)</td>
<td>Vial: 250, 500, 1000, 1500 IU and 2000 IU FVIII</td>
</tr>
<tr>
<td>Factor VIII/von Willebrand factor complex (Humate-P)</td>
<td>Vial: 250/600, 500/1200, 1000/2400 IU FVIII/VWF:RCo</td>
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<tr>
<td>Factor VIII/von Willebrand factor complex (Wilate)</td>
<td>Vial: 500/500, 1000/1000 IU FVIII/VWF:RCo</td>
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VII. References


Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Policy created</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
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<tbody>
<tr>
<td>4Q17 Annual Review</td>
<td>10.10.17</td>
<td>11.17</td>
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Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional
medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

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