Clinical Policy: Factor VIII/von Willebrand Factor Complex (Human – Alphanate, Humate-P, Wilate); von Willebrand Factor (Recombinant – Vonvendi)

Reference Number: LA.PHAR.216
Effective Date:
Last Review Date: 06.21 **Coding Implications**
Line of Business: Medicaid **Revision Log**

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) or recombinant von Willebrand factor requiring prior authorization: Alphanate®, Humate®-P, Vonvendi®, and Wilate®.

FDA Approved Indication(s)

Factor VIII/von Willebrand factor complexes are indicated for:

- **Hemophilia A**
  - **Alphanate: Control and prevention of bleeding episodes and perioperative management in adult and pediatric patients with factor VIII deficiency due to hemophilia A**
  - **Humate-P: Treatment and prevention of bleeding in adults with hemophilia A (classical hemophilia)**
  - **Wilate:**
    - **Control and prevention of bleeding episodes**
    - **Routine prophylaxis to reduce the frequency of bleeding episodes**
- **Von Willebrand disease (VWD) in children and adults:**
  - **Alphanate: Surgical and/or invasive procedures in patients in whom desmopressin (DDAVP) is either ineffective or contraindicated**
  - **Humate-P:**
    - **Treatment of spontaneous and trauma-induced bleeding episodes**
    - **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:**
    - **On-demand treatment and control of bleeding episodes**
    - **Perioperative management of bleeding**

Vonvendi is indicated in adults with VWD for:

- **On-demand treatment and control of bleeding episodes**
- **Perioperative management of bleeding**

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

Policy/Criteria
Prior authorization is required. Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of Louisiana Healthcare Connections that Alphanate, Humate-P, Vonvendi, and Wilate are medically necessary when the following criteria are met:

I. Initial Approval Criteria

A. Congenital Hemophilia A (must meet all):

1. **Diagnosis of congenital hemophilia A (factor VIII deficiency);**
2. **Request is for Alphanate, Humate-P, or Wilate;**
3. **Prescribed by or in consultation with a hematologist;**
4. **Request is for one of the following uses (a, b, or c):**
   a. **Control or prevention of bleeding episodes;**
   b. **Perioperative management (Alphanate only);**
   c. **Routine prophylaxis to reduce the frequency of bleeding episodes (Wilate only);**
5. **For routine prophylaxis requests (Wilate only), member meets one of the following (a or b):**
   a. **Member has severe hemophilia (defined as factor VIII level of < 1%);**
   b. **Member has experienced at least one life-threatening or serious spontaneous bleed (*see Appendix D*);**
6. **If factor VIII coagulant activity levels are > 5%, failure of desmopressin acetate, unless contraindicated, clinically significant adverse effects are experienced, or an appropriate formulation of desmopressin acetate is unavailable;**
7. **Documentation of member's current body weight (in kg);**
8. **Dose does not exceed the FDA approved maximum recommended dose for the relevant indication.**

Approval duration: 3 months

B. Von Willebrand Disease (must meet all):

1. **Diagnosis of VWD (types 1, 2, or 3);**
2. **Prescribed by or in consultation with a hematologist;**
3. **If diagnosis is VWD type 1 or 2 (except type 2B), then member has had a failure of desmopressin acetate, unless contraindicated, clinically significant adverse effects are experienced, or an appropriate formulation of desmopressin acetate is unavailable;**
4. **Request is for one of the following uses (a or b):**
   a. **Treatment of bleeding episodes (Humate-P, Vonvendi, and Wilate only);**
   b. **Perioperative management;**
5. **For Vonvendi only: age ≥ 18 years;**
6. **Documentation of member's current body weight (in kg);**
7. **Dose does not exceed the FDA approved maximum recommended dose for the relevant indication.**

Approval duration: 3 months

C. **Other diagnoses/indications**
   1. **Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): LA.PMN.53 for Medicaid.**

II. **Continued Therapy**
A. **All Indications in Section I (must meet all):**
   1. **Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;**
   2. **Member is responding positively to therapy;**
   3. **Documentation of member's current body weight (in kg);**
   4. **If request is for a dose increase, new dose does not exceed the FDA approved maximum recommended dose for the relevant indication.**

   Approval duration: 3 months

B. **Other diagnoses/indications (must meet 1 or 2):**
   1. **Currently receiving medication via Louisiana Healthcare Connections benefit and documentation supports positive response to therapy.**
      Approval duration: Duration of request or 3 months (whichever is less); or
   2. **Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): LA.PMN.53 for Medicaid.**

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 – LA.PMN.53 for Medicaid, 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
vWF: von Willebrand factor

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
desmopressin acetate (Stimate® nasal spray; generic	When Factor VIII coagulant activity levels are > 5% and for VWD type 1 or 2 (except 2B):	Injection: 0.3 mcg/kg IV every 48 hours

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
injection solution)	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	Nasal spray: 1 spray intranasally in each nostril

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.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): factor VIII/vWF complex: patients with known hypersensitivity reactions, including anaphylactic or severe systemic reaction, to human plasma-derived products, any ingredient in the formulation, or components of the container; Vonvendi: history of life-threatening hypersensitivity reactions to Vonvendi or its components
- Boxed warning(s): none reported

Appendix D: General Information

- Life-threatening bleeding episodes include, but are not limited to, bleeds in the following sites: intracranial, neck/throat, or gastrointestinal.
- Serious bleeding episodes include bleeds in the following site: joints (hemarthrosis).
- Spontaneous bleed is defined as a bleeding episode that occurs without apparent cause and is not the result of trauma.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
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 12 hours	100 IU/kg/day
Factor VIII/von Willebrand	Hemophilia A - control and prevention of	Minor episodes: 15 IU/kg IV loading dose followed by half of the loading dose given once or twice daily if needed	75 IU/kg/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
factor complex (Humate-P)	bleeding episodes	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	
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 IV loading dose followed by 40-50 IU/kg IV every 8-12 hours 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	240 IU/kg/day
Factor VIII/von Willebrand factor complex (Wilate)	Hemophilia A - control and prevention of bleeding episodes	Minor or moderate episodes: 30-40 IU/kg IV every 12-24 hours Major episodes: 35-50 IU/kg IV every 12-24 hours Life-threatening episodes: 35-50 IU/kg IV every 8-24 hours	150 IU/kg/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
Factor VIII/von Willebrand factor complex (Wilate)	Hemophilia A – routine prophylaxis	20-40 IU/kg IV every 2 to 3 days	40 IU/kg/day
Factor VIII/von Willebrand factor complex (Wilate)	VWD – control and prevention of bleeding episodes	Minor episodes: 20-40 IU/kg IV loading dose followed by 20-30 IU/kg every 12-24 hours Major episodes: 40-60 IU/kg IV loading dose followed by 20-40 IU/kg every 12-24 hours	60 IU/kg/day
Factor VIII/von Willebrand factor complex (Wilate)	VWD – perioperative management	Minor surgeries (including tooth extraction): 30-60 IU/kg IV loading dose followed by 15-30 IU/kg every 12-24 hours Major surgeries: 40-60 IU/kg IV loading dose followed by 20-40 IU/kg every 12-24 hours	60 IU/kg/day
von Willebrand factor (Vonvendi)	VWD – treatment and control of bleeding episodes	Minor episodes: 40-50 IU/kg IV loading dose followed by 40-50 IU/kg every 8-24 hours Major episodes: 50-80 IU/kg IV loading dose followed by 40-60 IU/kg every 8-24 hours for approximately 2 to 3 days	Minor episodes: 150 IU/kg/day Major episodes: 180 IU/kg/day
von Willebrand factor (Vonvendi)	VWD – perioperative management	Minor surgeries: 25-30 IU/kg IV every 12-48 hours Major surgeries: 40-60 IU/kg IV every 12-48 hours	Minor surgeries: 60 IU/kg/day Major surgeries: 120 IU/kg/day

VI. Product Availability

Drug Name	Availability
Factor VIII/von Willebrand factor complex (Alphanate)	Vial: 250, 500, 1,000, 1,500 IU and 2,000 IU FVIII
Factor VIII/von Willebrand factor complex (Humate-P)	Vial: 250/600, 500/1,200, 1,000/2,400 IU FVIII/VWF:RCo
von Willebrand factor (Vonvendi)	Vial: 450-850 IU (5 mL), 900-1,700 IU (10 mL)
Factor VIII/von Willebrand factor complex (Wilate)	Vial: 500/500, 1,000/1,000 IU FVIII/VWF:RCo

VII. References

1. Alphanate Prescribing Information. Los Angeles, CA: Grifols Biologicals Inc.; June 2018. Available at http://www.alphanate.com. Accessed December 1, 2020.
2. Humate-P Prescribing Information. Kankakee, IL: CSL Behring, LLC; September 2017. Available at http://www.humate-p.com. Accessed December 1, 2020.
3. Vonvendi Prescribing Information. Lexington, MA: Baxalta US Inc.; February 2019. Available at: https://www.shirecontent.com/PI/PDFs/VONVENDI_USA_ENG.pdf. Accessed December 1, 2020.
4. Wilate Prescribing Information. Hoboken, NJ: Octapharma USA Inc.; September 2019. Available at http://www.wilateusa.com. Accessed December 1, 2020.
5. Srivastava A, Brewer AK, Mauser-Bunschoten EP, et al. Guidelines for the management of hemophilia. Haemophilia. Jan 2013; 19(1): e1-47.
6. Medical and Scientific Advisory Council (MASAC) of the National Hemophilia Foundation (NHF): Database of treatment guidelines. Available at https://www.hemophilia.org/Researchers-Healthcare-Providers/Medical-and-Scientific-Advisory-Council-MASAC/MASAC-Recommendations. Accessed December 1, 2020.
7. MASAC of the NHF: Recommendations regarding the treatment of Von Willebrand disease. Available at: https://www.hemophilia.org/sites/default/files/document/files/244.pdf. Accessed December 1, 2020.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J7183	Injection, von Willebrand factor complex (human), Wilate, 1 IU vWF:RCo

HCPCS Codes	Description
J7186	Injection, antihemophilic factor VIII/von Willebrand factor complex (human), per factor VIII i.u. (Alphanate)
J7187	Injection, von Willebrand factor complex (Humate-P), per IU VWF:RCO
J7179	Injection, von Willebrand factor (recombinant), (Vonvendi), per 1 IU vWF:rco

Reviews, Revisions, and Approvals	Date
Converted corporate to local policy	06.2021

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. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. LHCC

retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom LHCC has no control or right of control. Providers are not agents or employees of LHCC.