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

Reference Number: CP.PHAR.216
Effective Date: 05.01.16
Last Review Date: 05.20
Line of Business: Commercial, HIM, Medicaid

Coding Implications
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) requiring prior authorization: Alphanate®, Humate®-P, 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

Limitation(s) of use:

- Alphanate is not indicated for patients with severe VWD (type 3) undergoing major surgery.

Policy/Criteria

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 health plans affiliated with Centene Corporation® that Alphanate, Humate-P, 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. Prescribed by or in consultation with a hematologist;
3. 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);
4. 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;
5. For Wilate only: member meets one of the following (a or b):
   a. Member has not received treatment with valoctocogene roxaparvovec;
   b. Request is for prophylaxis post-valoctocogene roxaparvovec gene therapy administration;
6. Dose does not exceed the FDA approved maximum recommended dose for the relevant indication.

Approval duration: 1 month (if immediately following valoctocogene roxaparvovec gene therapy administration) or 3 months (congenital hemophilia A with no valoctocogene roxaparvovec administration)

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. Request is for one of the following uses (a or b):
   a. Treatment of bleeding episodes (Humate-P and Wilate only);
   b. Perioperative management;
4. 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 for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. For Wilate only: member meets one of the following (a or b):
   a. Member is responding positively to therapy and has not received treatment with valoctocogene roxaparvovec;

b. Member is responding positively to therapy and request is for prophylaxis post-valoctocogene roxaparvovec gene therapy administration;

3. If request is for a dose increase, new dose does not exceed the FDA approved maximum recommended dose for the relevant indication.

Approval duration: 1 month (if immediately following valoctocogene roxaparvovec gene therapy administration) or 3 months (other indications)

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene 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 for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.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 – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.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

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
desmopressin acetate (Stimate® nasal spray; generic injection solution)	When Factor VIII coagulant activity levels are > 5% 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	Injection: 0.3 mcg/kg IV every 48 hours Nasal spray: 1 spray intranasally in each nostril

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	≥ 50 kg: 1 spray intranasally in each nostril; may repeat based on laboratory response and clinical condition	

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): 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
- Boxed warning(s): none reported

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 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	75 IU/kg/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
		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	Minor or moderate episodes: 30-40	150 IU/kg/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
	prevention of bleeding episodes	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	
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

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

Drug Name	Availability
Factor VIII/von Willebrand factor complex (Humate-P)	Vial: 250/600, 500/1,200, 1,000/2,400 IU FVIII/VWF:RCo
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 November 27, 2019.
2. Humate-P Prescribing Information. Kankakee, IL: CSL Behring, LLC; September 2017. Available at http://www.humate-p.com. Accessed November 27, 2019.
3. Wilate Prescribing Information. Hoboken, NJ: Octapharma USA Inc.; September 2019. Available at http://www.wilateusa.com. Accessed November 27, 2019.
4. Srivastava A, Brewer AK, Mauser-Bunschoten EP, et al. Guidelines for the management of hemophilia. Haemophilia. Jan 2013; 19(1): e1-47.
5. 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 November 27, 2019.

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
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

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy split from CP.PHAR.12.Blood Factors and converted to new template. Removed requests for documentation. Removed indication for prophylaxis after 2 joint bleeds/approval period 6 months as there is no FDA approved indication for long-term prophylaxis. Approval period is edited to be 3 months initial and one 3-month re-auth as, in some circumstances, treatment could be necessary for up to six months (e.g., intracranial hemorrhage per Alphanate PI). Reviewed by specialist.	04.01.16	05.16

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Removed "major surgery" restriction for Alphanate. Required trial of desmopressin is edited to avoid necessity of testing for coagulation factors. Safety information removed. Uses and approval periods across all blood factor policies worded consistently. Efficacy statement added to renewal criteria. Hemophilias are specified as "congenital" versus "acquired" across blood factor policies where indicated. Reviewed by specialist- hematology/internal medicine	04.01.17	05.17
1Q18 annual review: - Converted to new template -No significant changes - References reviewed and updated.	11.27.17	02.18
1Q 2019 annual review: added HIM-Medical Benefit; no significant changes; references reviewed and updated.	09.26.18	02.19
1Q 2020 annual review: no significant changes; added HIM line of business; RT4 policy update addition of hemophilia A indication for Wilate, mirroring previously approved hemophilia A coverage policies for other FVIII products; references reviewed and updated.	11.27.19	02.20
Added Commercial line of business.	03.13.20	
Added 1 month approval duration for use post-valoctocogene gene therapy administration in hemophilia A for Wilate only.	04.17.20	05.20

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. The Health Plan 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. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

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 Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. 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. The Health Plan 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 the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.