

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

Reference Number: DE.PHAR.216

Effective Date: 01.23

Last Review Date: 01.23

Line of Business: 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) or recombinant von Willebrand factor requiring prior authorization: Alphanate<sup>®</sup>, Humate<sup>®</sup>-P, Vonvendi<sup>®</sup>, and Wilate<sup>®</sup>.

### **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
- Routine prophylaxis to reduce the frequency of bleeding episodes in patients with severe Type 3 von Willebrand disease receiving on-demand therapy

## CLINICAL POLICY

### Factor VIII/von Willebrand Factor Complex; von Willebrand Factor

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, 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), for members who have not previously used Wilate for routine prophylaxis, 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 one of the following (a or b):
  - a. VWD type 1 or 2 (except type 2B), and 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;
  - b. VWD type 2B or 3;
2. Prescribed by or in consultation with a hematologist;
3. For Vonvendi only: age  $\geq$  18 years;
4. For Vonvendi only: Failure of an adequate trial of at least two preferred\* FDA-approved drugs for the indication and/or drugs that are considered the standard of care within the same drug class on the PDL, when such agents exist, at maximum indicated doses, unless clinically significant adverse effect are experienced, or all are contraindicated;

*\*Generic is preferred, if available, and brand is not the preferred agent*

## CLINICAL POLICY

### Factor VIII/von Willebrand Factor Complex; von Willebrand Factor

5. Request is for one of the following uses (a, b, or c):
  - a. Treatment of bleeding episodes (Humate-P, Vonvendi, and Wilate only);
  - b. Perioperative management;
  - c. Routine prophylaxis to reduce the frequency of bleeding episodes in patients with severe VWD type 3 receiving on-demand therapy (Vonvendi only);
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 for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53.

## 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. 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 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.PMN.53.

## 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.PMN.53 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*

## CLINICAL POLICY

### Factor VIII/von Willebrand Factor Complex; von Willebrand Factor

*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 <sup>®</sup> nasal spray; generic injection solution)	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  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	Injection: 0.3 mcg/kg IV every 48 hours  Nasal spray: 1 spray intranasally in each nostril
Hemlibra (emicizumab-kxwh)	3 mg/kg per week IV during the first four weeks of therapy, followed by either 1.5 mg/kg per week, 3 mg/kg once every two weeks, or 6 mg/kg once every four weeks thereafter	6 mg/kg/month

*Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) 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	Hemophilia A - control and prevention of	Minor episodes: 15 IU/kg IV every 12 hours	100 IU/kg/day

## CLINICAL POLICY

### Factor VIII/von Willebrand Factor Complex; von Willebrand Factor

Drug Name	Indication	Dosing Regimen	Maximum Dose
factor complex (Alphanate)	bleeding episodes	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	
Factor VIII/von Willebrand factor complex (Humate-P)	Hemophilia A - control and prevention of bleeding episodes	Minor episodes: 15 IU/kg IV loading dose 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  Moderate episodes: 25 IU/kg IV loading dose to achieve a FVIII:C plasma level of approximately 50% of normal, followed by 15 IU/kg IV 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 episodes: 40-50 IU/kg IV initially followed by 20-25 IU/kg IV 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.	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	<u>Type 1 VWD, mild disease</u> Minor or major episodes: 40-60 IU/kg IV loading dose followed by 40-50 IU/kg IV every 8-12 hours for 3 days to keep the trough level of VWF:RCo > 50%. Then 40-50 IU/kg daily for up to 7 days.  <u>Type 1 VWD, moderate or severe disease</u> Minor episodes: 40-50 IU/kg IV as one or two doses	240 IU/kg/day

## CLINICAL POLICY

### Factor VIII/von Willebrand Factor Complex; von Willebrand Factor

Drug Name	Indication	Dosing Regimen	Maximum Dose
		<p>Major episodes: 50-75 IU/kg loading dose followed by 40-60 IU/kg every 8-12 hours for 3 days to keep the trough level of VWF:RCo &gt; 50%. Then 40-60 IU/kg daily for up to 7 days.</p> <p><u>Type 2 or 3 VWD</u>                      Minor episodes: 40-50 IU/kg IV as one or two doses</p> <p>Major episodes: 60-80 IU/kg IV loading dose followed by 40-60 IU/kg every 8-12 hours for 3 days to keep the trough level of VWF:RCo &gt; 50%. Then 40-60 IU/kg daily for up to 7 days.</p>	
Factor VIII/von Willebrand factor complex (Wilate)	Hemophilia A - control and prevention of bleeding episodes	<p>Minor or moderate episodes: 30-40 IU/kg IV every 12-24 hours</p> <p>Major episodes: 35-50 IU/kg IV every 12-24 hours</p> <p>Life-threatening episodes: 35-50 IU/kg IV every 8-24 hours</p>	150 IU/kg/day
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	<p>Minor episodes: 20-40 IU/kg IV loading dose followed by 20-30 IU/kg every 12-24 hours</p> <p>Major episodes: 40-60 IU/kg IV loading dose followed by 20-40 IU/kg every 12-24 hours</p>	60 IU/kg/day
Factor VIII/von Willebrand factor complex (Wilate)	VWD – perioperative management	<p>Minor surgeries (including tooth extraction): 30-60 IU/kg IV loading dose followed by 15-30 IU/kg every 12-24 hours</p> <p>Major surgeries: 40-60 IU/kg IV loading dose followed by 20-40 IU/kg every 12-24 hours</p>	60 IU/kg/day

## CLINICAL POLICY

### Factor VIII/von Willebrand Factor Complex; von Willebrand Factor

Drug Name	Indication	Dosing Regimen	Maximum Dose
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
von Willebrand factor (Vonvendi)	VWD- Routine prophylaxis to reduce the frequency of bleeding episodes in patients with severe type 3 VWD receiving on-demand therapy	Initiation of prophylactic treatment: 40-60 IU/kg IV twice weekly	60 IU/kg twice weekly

#### VI. Product Availability

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

## CLINICAL POLICY

### Factor VIII/von Willebrand Factor Complex; von Willebrand Factor

Drug Name	Availability
Factor VIII/von Willebrand factor complex (Wilate)	Vials: 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, 2021.
2. Humate-P Prescribing Information. Kankakee, IL: CSL Behring, LLC; June 2020. Available at <http://www.humate-p.com>. Accessed November 27, 2021.
3. Vonvendi Prescribing Information. Lexington, MA: Baxalta US Inc.; January 2022. Available at: [https://www.shirecontent.com/PI/PDFs/VONVENDI\\_USA\\_ENG.pdf](https://www.shirecontent.com/PI/PDFs/VONVENDI_USA_ENG.pdf). Accessed March 15, 2022.
4. Wilate Prescribing Information. Hoboken, NJ: Octapharma USA Inc.; September 2019. Available at <http://www.wilateusa.com>. Accessed November 27, 2021.
5. Srivastava A, Santagostino E, Dougall A, et al. WFH guidelines for the management of hemophilia. *Haemophilia*. 2020;26(suppl 6):1-158.
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
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	P&T Approval Date
Policy created	11.22	01.23

#### 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



## CLINICAL POLICY

### Factor VIII/von Willebrand Factor Complex; von Willebrand Factor

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.

## **CLINICAL POLICY**

### **Factor VIII/von Willebrand Factor Complex; von Willebrand Factor**

Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

©2016 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene® and Centene Corporation® are registered trademarks exclusively owned by Centene Corporation.