Factor VIII/VWF Complex: Alphanate®, Humate-P®, and Wilate®

Date of Origin: 01/22/2020 **Last Review Date: 01/22/2020** **Effective Date: 02/01/2020**

Dates Reviewed: 01/22/2020

Developed By: Medical Criteria Committee

I. Length of Authorization

- Initial: 6 months (for on-demand and prophylaxis); 1 month (for perioperative)
- Renewal: 12 months (for prophylaxis); 6 months (for on-demand)

II. Dosing Limits

Product Name	Dosage Form	Indication/ FDA Labeled Dosing	Quantity Limit‡
Alphanate, antihemophilic factor/von Willebrand factor complex (human)	250, 500, 1000, 1500, 2000 IU FVIII	**Control and prevention of bleeding – hemophilia A**[δ]: Up to 50 IU factor VIII/kg twice daily for at least three to five days. Following this, factor VIII levels should be maintained at 25 IU factor VIII/kg twice daily until healing has been achieved. Major hemorrhages may require treatment for up to ten days. Intracranial hemorrhages may require prophylaxis therapy for up to six months.	**Control and prevention of bleeding in hemophilia A:** Up to the number of doses requested every 28 days
		Perioperative management – hemophilia A: Up to 50 IU factor VIII/kg prior to surgery, then up to 50 IU factor VIII/kg twice daily for the next seven to ten days, or until healing has been achieved	**Perioperative management in hemophilia A:** Up to the number of doses requested for 28 days
		Control and prevention of bleeding and perioperative management – vWD[γ]: Pre-operative/pre-procedure dose: • Adults: Up to 60 IU VWF:RCo/kg body weight • Pediatrics: Up to 75 IU VWF:RCo/kg body weight Maintenance: • Adults: Up to 60 IU VWF:RCo/kg body weight at eight to 12 hour intervals as	**Control and prevention of bleeding and perioperative management in vWD:** Up to the number of doses requested for 28 days

		clinically needed for at least three to seven days • Pediatrics: Up to 75 IU VWF:RCo/kg body weight at eight to 12 hour intervals as clinically needed for at least three to seven days	
Humate-P, antihemophilic factor/von Willebrand factor complex (human)	600, 1200, 2400 IU vWF:RCo	**Control and prevention of bleeding – hemophilia A*:** • Minor: Up to 15 IU factor VIII:C/kg to achieve a factor VIII: C plasma level of approximately 30% of normal. One infusion may be sufficient. If needed, half of the loading dose may be given one or twice daily for one to two days • Moderate: Up to 25 15 IU factor VIII:C/kg to achieve a factor VIII: C plasma level of approximately 50% of normal, followed by 15 IU factor VIII:C/kg every eight to 12 hours for the first one to two days to maintain the factor VIII:C plasma level at 30% of normal. Continue the same dose one or twice for up to seven days or until adequate wound healing is achieved • Major: Initially up to 50 IU factor VIII:C/kg, followed by up to 25 IU factor VIII:C/kg every eight hours to maintain the factor VIII:C plasma level at 80-100% of normal for seven days. Continue the same dose one or twice daily for another seven days to maintain the factor VIII:C level at 30-50% of normal **Control and prevention of bleeding – vWD:** Up to 80 IU vWF:RCo (corresponding to 17 to 33 IU factor VIII in Humate-P) per kg body weight every eight to 12 hours. Adjust as needed based on the extent and location of bleeding. Repeat doses as long as necessary. **Perioperative management – vWD:** <u>Loading</u>: • Major: vWF:RCo target peak plasma level – 100 IU/dL; Target factor VIII:C activity – 80-100 IU/dL	**Control and prevention of bleeding – hemophilia A:** Up to the number of doses requested every 28 days **Control and prevention of bleeding – vWD:** Up to the number of doses requested every 28 days **Perioperative management – vWD:** Up to the number of doses requested for 28 days

		• Minor: vWF:RCo target peak plasma level – 50-60 IU/dL; Target factor VIII:C activity – 40-50 IU/dL • Emergency: vWF:RCo target peak plasma level – 100 IU/dL; Target factor VIII:C activity – 80-100 IU/dL. Administer a dose of 50-60 IU vWF:RCo/kg body weight <u>Maintenance</u>: Initial maintenance dose should be half the loading dose, irrespective of additional dosing required to meet factor VIII:C targets. Subsequent doses should be based on the patient's vWF:RCo and factor VIII levels	
Wilate, von Willebrand factor/coagulation factor VIII complex (human)		**Control of bleeding episodes – vWD**[€]: Up to 60 IU/kg initially, followed by up to 40 IU/kg every 12 to 24 hours until vWF:Rco and factor VIII activity trough levels > 50%, for up to five to seven days **Perioperative management of bleeding – vWD**: Up to 60 IU/kg initially, followed by up to 40 IU/kg every 12 to 24 hours until wound healing achieved, up to six days or more. vWF:Rco and factor VIII activity trough levels > 50% and peak levels 100% until wound healing is achieved, up to six days or more	**Control of bleeding episodes – vWD:** Up to the number of doses requested every 28 days **Perioperative management of bleeding – vWD:** Up to the number of doses requested for 28 days

[‡]Allows for +5% to account for assay and vial availability

[δ] Dose (IU) = body weight (kg) x desired factor VIII rise (IU/dL or % normal) x 0.5 (IU/kg per IU/dL)

[ɣ] The ratio of VWF:RCo to factor VIII varies by lot, so with each new lot, check the IU vWF:RCo/Vial to ensure accurate dosing

[*] One IU of factor VIII activity per kg body weight will increase the circulating factor VIII level by approximately 2 IU/dL

[Ψ] Target peak plasma vWF:RCo level – baseline plasma vWF:RCo level) – body weight (kg)/in vivo recovery. If the in vivo recovery is not available, assume an in vivo recovery of 2 IU/dL per IU/kg and calculate the loading dose as follows: (100 – baseline plasma vWF:RCo) x body weight (kg)/2

[€] The ratio between vWF:RCo and factor VIII activities is approximately 1:1. The dosage should be adjusted according to the extent and location of the bleeding.

III. Initial Approval Criteria

<u>von Willebrand Disease</u>

I. **Alphanate** or **Humate-P** may be considered medically necessary when the following criteria below are met:
   A. Treatment is prescribed by or in consultation with a hematologists; **AND**

B. A diagnosis of von Willebrand disease (vWD) has been confirmed by blood coagulation and von Willebrand factor testing; **AND**
C. Use is planned for one of the following indications:
    1. Treatment of spontaneous and trauma-induced bleeding episodes; **OR**
    2. Used as surgical bleeding prophylaxis during major or minor procedures when desmopressin (DDAVP) is either ineffective or contraindicated; **AND**
    3. **Alphanate** will not be used for severe (type 3) vWD undergoing major surgery

II. **Wilate** may be considered medically necessary when the following criteria below are met:
A. Treatment is prescribed by or in consultation with a hematologists; **AND**
B. A diagnosis of von Willebrand disease (vWD) has been confirmed by blood coagulation and von Willebrand factor testing; **AND**
C. Use is planned for one of the following indications:
    1. Perioperative management of bleeding; **OR**
    2. For the treatment of spontaneous and trauma-induced bleeding episodes when one of the following is met:
        i. Member has severe vWD; **OR**
        ii. Member has mild or moderate vWD and the use of desmopressin (DDAVP) is known or suspected to be ineffective or contraindicated; **AND**
D. Wilate will not be used for the routine prophylactic treatment of spontaneous bleeding episodes; **AND**
E. Wilate is not being used for hemophilia A

Hemophilia A (congenital factor VIII deficiency)

I. **Alphanate** or **Humate-P** may be considered medically necessary when the following criteria below are met:
A. Treatment is prescribed by or in consultation with a hematologist; **AND**
B. A diagnosis of hemophilia A has been confirmed by blood coagulation testing; **AND**
C. Use is planned for one of the following indications:
    1. On-demand treatment and control of bleeding episodes **AND** the number of factor VIII/VWF units requested does not exceed those outlined in the Quantity Limits table above for routine prophylaxis; **OR**
    2. Routine prophylaxis to reduce the frequency of bleeding episodes when one of the following is met:
        i. Member has severe hemophilia A (defined as factor VIII level of <1%); **OR**
        ii. Member has had more than one documented episode of spontaneous bleeding; **OR**
    3. Perioperative management of bleeding; **AND**
D. Documentation that inhibitor testing has been performed within the last 12 months AND if inhibitor titers are high (≥5 Bethesda units), there is a documented plan to address inhibitors; **AND**
E. Dose and frequency does not exceed those outlined in the Quantity Limit Table above, unless documented clinical reasoning for higher dosing and/or frequency is supported by a half-life study to determine the appropriate dose and dosing interval

II. Alphanate, Humate-P, and Wilate are considered investigational when used for any other condition.

III. Renewal Criteria

I. Documentation of clinical benefit, including decreased incidence of bleeding episodes or stability of bleeding episodes relative to baseline

VI. Billing Code/Availability Information

Drug	Manufacturer	J-Code	1 Billable Unit Equiv.	Vial Size	NDC
Alphanate	Grifols Biologicals Inc	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	J7183	1 IU VWF:RCO	500 units	67467-0182
				1000 units	

VII. References

1. Alphanate® [Prescribing Information]. Los Angeles, CA: Grifols; June 2018
2. Humate-P® [Prescribing Information]. Kankakee, IL; CSL Behring LLC; September 2017
3. Wilate® [Prescribing Information]. Hoboken, NJ; Octapharm USA; September 2016
4. National Hemophilia Foundation. MASAC Recommendations Concerning products Licensed for the Treatment of Hemophilia and Other Bleeding Disorders. Available from: https://www.hemophilia.org/Researchers-Healthcare-Providers/Medical-and-Scientific-Advisory-Council-MASAC/MASAC-Recommendations. Accessed July 5, 2019.
5. UpToDate, Inc. Hemophilia A and B: Routine management including prophylaxisTreatment of von Willebrand disease. UpToDate [database online]. Last updated July 19, 2019.
6. National Hemophilia Foundation. Hemophilia A. Available from: https://www.hemophilia.org/Bleeding-Disorders/Types-of-Bleeding-Disorders/Hemophilia-A. Accessed July 5, 2019.

7. National Hemophilia Foundation. MASAC Recommendations Concerning products Licensed for the Treatment of Hemophilia and Other Bleeding Disorders. Available from: https://www.hemophilia.org/Researchers-Healthcare-Providers/Medical-and-Scientific-Advisory-Council-MASAC/MASAC-Recommendations. Accessed July 5, 2019.
8. UpToDate, Inc. Hemophilia A and B: Routine management including prophylaxisHemophilia A and B: Routine management including prophylaxis. UpToDate [database online]. Last updated February 11, 2019.

Appendix 1 – Covered Diagnosis Codes

Alphanate, Humate-P

ICD-10	ICD-10 Description
D66	Hereditary factor VIII deficiency
D68.0	Von Willebrand's disease

Wilate

ICD-10	ICD-10 Description
D68.0	Von Willebrand's disease

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA,HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corporation (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corporation (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.

J (10)	TN, GA, AL	Cahaba Government Benefit Administrators, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC