Properties of treatment options for von Willebrand disease (VWD)

Alphanate®
antihemophilic factor/von Willebrand factor complex (human)

VON WILLEBRAND DISEASE THERAPIES

	PLASMA-DERIVED VWF			RECOMBINANT VWF
BRAND NAME	**ALPHANATE**	**Humate-P®**	**Wilate®**	**Vonvendi®**
Generic name	Antihemophilic Factor/von Willebrand Factor Complex (Human)	Antihemophilic Factor/von Willebrand Factor Complex (Human)	von Willebrand Factor/ Coagulation Factor VIII Complex (Human)	von Willebrand Factor (Recombinant)
VWD indication	Indicated for surgical and/or invasive procedures in adult and pediatric patients with VWD in whom DDAVP is either ineffective or contraindicated. It is not indicated for patients with severe VWD (type 3) undergoing major surgery	Indicated in adults and pediatric patients with VWD for: 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	Indicated in children and adults with VWD for: on-demand treatment and control of bleeding episodes; perioperative management of bleeding	Indicated for on-demand treatment and control of bleeding episodes in adults diagnosed with VWD
Hemophilia A indication	Indicated for control and prevention of bleeding episodes and perioperative management in adult and pediatric patients with FVIII deficiency due to hemophilia A	Indicated for treatment and prevention of bleeding in adults with hemophilia A	None	None
Half-life (hours)	VWF:RCo 7.67; FVIII 21.58	VWF:RCo 10-11; FVIII 12.2	VWF:RCo 15.8; FVIII 19.6	19.1-21.9
Licensure date	1997	1986	2009	2015
VWF:RCo/FVIII ratio	1.2:1	2.4:1	1:1	N/A
Reconstitution volume	5 mL for 250 and 500 IU FVIII; 10 mL for 1000, 1500, 2000 IU FVIII	5 mL for 250 IU; 10 mL for 500 IU; 15 mL for 1000 IU	5 mL for 500 IU VWF:RCo and IU FVIII; 10 mL for 1000 IU VWF:RCo and IU FVIII	5 mL for 450-850 IU VWF:RCo; 10 mL for 900-1700 IU VWF:RCo
Infusion rate	Infuse intravenously at a maximum rate of 10 mL/min	Slowly infuse intravenously at a maximum rate of 4 mL/min	Inject intravenously at a slow speed of 2-4 mL/min	Infuse intravenously at a rate that ensures the comfort of the patient, up to a maximum of 4 mL/min
Virus inactivation/ removal methods	Affinity chromatography, solvent/detergent, dry heat treatment	Cryoprecipitation; Al(OH)3 adsorption, glycine precipitation, NaCl precipitation, heat treatment, lyophilization	Solvent/detergent, dry heat treatment, ion-exchange chromatography	Immunoaffinity chromatography
Prion elimination steps	3.5% PEG precipitation, affinity chromatography, saline precipitation	N/A	N/A	N/A
Vial sizes	250, 500, 1000, 1500, 2000 IU FVIII; or 300, 600, 1200, 1800, 2400 IU VWF:RCo/vial	250, 500, 1000 IU FVIII/vial; or 600, 1200, 2400 IU VWF:RCo/vial	500, 1000 IU VWF:RCo and FVIII	450-850; 900-1700 IU VWF:RCo
Storage	Storage temp should not exceed 77°F. Stable for 36 months up to expiration date. Do not freeze	Storage temp should not exceed 77°F. Stable for 36 months up to expiration date. Do not freeze	Store refrigerated for up to 36 months; do not freeze. May store at a maximum room temperature of 77°F for up to 6 months; do not return to refrigerator once stored at room temperature	Store refrigerated; do not freeze. May store at a maximum room temperature of 86°F for up to 12 months; do not return to refrigerator once stored at room temperature
Manufacturer	Grifols	CSL Behring	Octapharma	Shire

ALPHANATE is contraindicated in patients who have manifested life-threatening immediate hypersensitivity reactions, including anaphylaxis, to the product or its components.

Anaphylaxis and severe hypersensitivity reactions are possible with ALPHANATE. Discontinue use of ALPHANATE if hypersensitivity symptoms occur, and initiate appropriate treatment.

Please see Important Safety Information on page 4 and accompanying full Prescribing Information for ALPHANATE at www.alphanate.com.

Properties of plasma-derived treatment options for hemophilia A

Alphanate®
antihemophilic factor/von Willebrand factor complex (human)

HEMOPHILIA A THERAPIES

	PLASMA-DERIVED FACTOR VIII				
BRAND NAME	**ALPHANATE**	**Humate-P®**	**Hemofil® M**	**Koate®**	**Monoclate-P®**
Generic name	Antihemophilic Factor/ von Willebrand Factor Complex (Human)	Antihemophilic Factor/ von Willebrand Factor Complex (Human)	Antihemophilic Factor (Human), Method M, Monoclonal Purified Nanofiltered	Antihemophilic Factor (Human)	Antihemophilic Factor (Human)
Hemophilia A indication	Indicated for control and prevention of bleeding episodes and perioperative management in adult and pediatric patients with FVIII deficiency due to hemophilia A	Indicated for treatment and prevention of bleeding in adults with hemophilia A	Indicated in hemophilia A for the prevention and control of hemorrhagic episodes	Indicated for the control and prevention of bleeding episodes or in order to perform emergency and elective surgery in patients with hemophilia A	Indicated for the treatment of classical hemophilia (hemophilia A), including surgery and surgical prophylaxis
VWD indication	Indicated for surgical and/or invasive procedures in adult and pediatric patients with VWD in whom DDAVP is either ineffective or contraindicated. It is not indicated for patients with severe VWD (type 3) undergoing major surgery	Indicated in adults and pediatric patients with VWD for: 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	None	None	None
Half-life (hours)	17.9	12.2	14.8	16.1	17.5
Licensure date	1997	1986	1988	1999	1990
Type of plasma derived	FVIII/VWF	FVIII/VWF	FVIII	FVIII/VWF	FVIII
Reconstitution volume	5 mL for 250 and 500 IU FVIII; 10 mL for 1000, 1500, 2000 IU FVIII	5 mL for 250 IU FVIII; 10 mL for 500 IU FVIII; 15 mL for 1000 IU FVIII	10 mL for all vial sizes	5 mL for 250, 500 IU FVIII; 10 mL for 1000 IU FVIII	2.5 mL for 250 IU FVIII; 5 mL for 500 IU FVIII; 10 mL for 1000, 1500 IU FVIII
Infusion rate	Infuse intravenously at a maximum rate of 10 mL/min	Slowly infuse intravenously at a maximum rate of 4 mL/min	Infuse intravenously at a rate comfortable to the patient, up to 10 mL/min	Administer intravenously at a rate of up to 5 mL/min to 10 mL/min	Administer intravenously at a rate comfortable to patient, approx. 2 mL/min
Virus inactivation/ removal methods	Affinity chromatography, solvent/detergent, dry heat treatment	Cryoprecipitation, Al(OH)3 adsorption, glycine precipitation, and NaCl precipitation, heat treatment	Affinity chromatography, ion-exchange chromatography, solvent/detergent, nanofiltration	Solvent-detergent, heat treatment, PEG precipitation/depth filtration	Pasteurization, heat treatment
Prion elimination steps	3.5% PEG precipitation, affinity chromatography, saline precipitation	N/A	N/A	Gel permeation chromatography	N/A
Vial sizes	250, 500, 1000, 1500, 2000 IU FVIII	250, 500, 1000 IU FVIII or 600, 1200, 2400 IU VWF:RCo	250, 500, 1000, 1700 IU FVIII	250, 500, 1000 IU FVIII	250, 500, 1000, 1500 IU FVIII
Storage	Storage temp should not exceed 77°F. Stable for 36 months up to expiration date. Do not freeze	Storage temp should not exceed 77°F. Stable for 36 months up to expiration date. Do not freeze	Store refrigerated; do not freeze. May store at a maximum room temperature of 86°F until expiration date	Store refrigerated; do not freeze. May store at a maximum room temperature of 77°F for up to 6 months	Store refrigerated; do not freeze. May store at a maximum room temperature of 77°F for up to 6 months
Manufacturer	Grifols	CSL Behring	Shire	Manufactured by Grifols; distributed by Kedrion	CSL Behring

Please see Important Safety Information on page 4 and accompanying full Prescribing Information for ALPHANATE at www.alphanate.com.

Properties of recombinant treatment options for hemophilia A

HEMOPHILIA A THERAPIES

Alphanate®
antihemophilic factor/von Willebrand factor complex (human)

RECOMBINANT FACTOR VIII

BRAND NAME	Advate®	Adynovate®	Afstyla®	Eloctate®	Kovaltry®	NovoEight®	Nuwiq®	Xyntha®
Generic name	Antihemophilic Factor (Recombinant)	Antihemophilic Factor (Recombinant), PEGylated	Antihemophilic Factor (Recombinant), Single Chain	Antihemophilic Factor (Recombinant), Fc Fusion Protein	Antihemophilic Factor (Recombinant)	Antihemophilic Factor (Recombinant)	Antihemophilic Factor (Recombinant)	Antihemophilic Factor (Recombinant)
Hemophilia A indication	Indicated for use in children and adults with hemophilia A for: control and prevention of bleeding episodes; perioperative management; routine prophylaxis to prevent or reduce the frequency of bleeding episodes	Indicated in children and adults with hemophilia A for: on-demand treatment and control of bleeding episodes; perioperative management; routine prophylaxis to reduce the frequency of bleeding episodes	Indicated in children and adults with hemophilia A for: on-demand treatment and control of bleeding episodes; routine prophylaxis to reduce the frequency of bleeding episodes; perioperative management of bleeding	Indicated in adults and children with hemophilia A for: on-demand treatment and control of bleeding episodes; perioperative management of bleeding; routine prophylaxis to reduce the frequency of bleeding episodes	Indicated in children and adults with hemophilia A for: on-demand treatment and control of bleeding episodes; perioperative management of bleeding; routine prophylaxis to reduce the frequency of bleeding episodes	Indicated in adults and children with hemophilia A for: control and prevention of bleeding episodes; perioperative management; routine prophylaxis to prevent or reduce the frequency of bleeding episodes	Indicated in children and adults with hemophilia A for: on-demand treatment and control of bleeding episodes; perioperative management of bleeding; routine prophylaxis to reduce the frequency of bleeding episodes	Indicated in adults and children with hemophilia A for: control and prevention of bleeding episodes; perioperative management
VWD indication	None	None	None	None	None	None	None	None
Half-life (hours)	12.0 in adults and adolescents; 8.7-11.2 in children	14.7 in adults; 13.4 in adolescents; 11.8-12.4 in children	14.2 in adults; 14.3 in adolescents; 10.2-10.4 in children	19.7 in adults; 16.4 in adolescents; 12.7-14.9 in children	14.2-14.3 in adults; 11.7-14.4 in adolescents; 12.0-12.1 in children	10.8-12 in adults and adolescents; 7.7-10.0 in children	17.1 in adults and adolescents; 11.9-13.1 in children	11.2 in adults and adolescents; 6.9-8.3 in children and adolescents
Licensure date	2003	2015	2016	2014	2016	2013	2015	2008
Reconstitution volume	2 mL for 250, 500, 1000, 1500 IU FVIII; 5 mL for 2000, 3000, 4000 IU FVIII	2 mL or 5 mL for 250, 500, 750, 1000, 1500 IU FVIII; 5 mL for 2000, 3000 IU FVIII	2.5 mL for 250, 500, 1000 IU FVIII; 5 mL for 1500, 2000, 2500, 3000 IU FVIII	3 mL for all vial sizes	2.5 mL for 250, 500, 1000 IU FVIII; 5 mL for 2000, 3000 IU FVIII	4 mL for all vial sizes	2.5 mL for all vial sizes	4 mL for all vial sizes
Infusion rate	Administer intravenously over a period of ≤5 min; maximum infusion rate 10 mL/min	Inject intravenously over a period of ≤5 min; maximum infusion rate 10 mL/min	Administer intravenously at a rate comfortable to the patient, up to 10 mL/min	Infuse intravenously at a maximum rate of 10 mL/min	Administer intravenously over a period of 1 to 15 min	Inject intravenously slowly over 2 to 5 min	Infuse intravenously at a maximum rate of 4 mL/min	Inject intravenously over several minutes
Virus inactivation/ removal methods	Immunoaffinity chromatography; solvent/detergent	Immunoaffinity chromatography; solvent/detergent	Solvent/detergent; nanofiltration (20 nm)	Detergent; nanofiltration (15 nm)	Solvent/detergent; nanofiltration (20 nm)	Immunoaffinity chromatography; solvent/detergent; nanofiltration (20 nm)	Chromatography; solvent/detergent; nanofiltration (20 nm)	Affinity chromatography; solvent/detergent; nanofiltration
Prion elimination steps	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Vial sizes (IU FVIII)	250, 500, 1000, 1500, 2000, 3000, 4000	250, 500, 750, 1000, 1500, 2000, 3000	250, 500, 1000, 1500, 2000, 2500, 3000	250, 500, 750, 1000, 1500, 2000, 3000, 4000, 5000, 6000	250, 500, 1000, 2000, 3000	250, 500, 1000, 1500, 2000, 3000	250, 500, 1000, 2000, 2500, 3000, 4000	250, 500, 1000, 2000
Storage	Store refrigerated; do not freeze. May store at a maximum room temperature of 86°F for up to 6 months; do not return to refrigerator after room temperature storage	Store refrigerated; do not freeze. May store at a maximum room temperature of 86°F for up to 3 months; do not return to refrigerator after room temperature storage	Store refrigerated; do not freeze. May store at a maximum room temperature of 77°F for up to 3 months; do not return to refrigerator after room temperature storage	Store refrigerated; do not freeze. May store at a maximum room temperature of 86°F for up to 6 months; do not return to refrigerator after room temperature storage	Store refrigerated for up to 30 months; do not freeze. May store at a maximum room temperature of 77°F for up to 12 months; do not return to refrigerator after room temperature storage	Store refrigerated for up to 30 months; do not freeze. May store at a maximum room temperature of 86°F for up to 12 months; do not return to refrigerator after room temperature storage	Store refrigerated for up to 24 months; do not freeze. May store at a maximum room temperature of 77°F for up to 3 months; do not return to refrigerator after room temperature storage	Store refrigerated for up to 36 months; do not freeze. May store at a maximum room temperature of 77°F for up to 3 months. Can be returned to refrigerator after room temperature storage no more than once
Manufacturer	Shire	Shire	CSL Behring	Bioverativ	Bayer	Novo Nordisk	Octapharma	Pfizer

The most frequent adverse drug reactions reported with ALPHANATE in >1% of infusions were pruritus, headache, back pain, paresthesia, respiratory distress, facial edema, pain, rash, and chills.

More than 1.8 billion units of ALPHANATE have been infused worldwide

Indications

ALPHANATE® (antihemophilic factor/von Willebrand factor complex [human]) is indicated for:

- Control and prevention of bleeding episodes and perioperative management in adult and pediatric patients with factor VIII (FVIII) deficiency due to hemophilia A
- Surgical and/or invasive procedures in adult and pediatric patients with von Willebrand disease (VWD) in whom desmopressin (DDAVP) is either ineffective or contraindicated. It is not indicated for patients with VWD (type 3) undergoing major surgery

Important Safety Information

ALPHANATE is contraindicated in patients who have manifested life-threatening immediate hypersensitivity reactions, including anaphylaxis, to the product or its components.

Anaphylaxis and severe hypersensitivity reactions are possible with ALPHANATE. Discontinue use of ALPHANATE if hypersensitivity symptoms occur, and initiate appropriate treatment.

Development of procoagulant activity-neutralizing antibodies (inhibitors) has been detected in patients receiving FVIII-containing products. Carefully monitor patients treated with AHF products for the development of FVIII inhibitors by appropriate clinical observations and laboratory tests.

Thromboembolic events have been reported with AHF/VWF complex (human) in VWD patients, especially in the setting of known risk factors.

Intravascular hemolysis may occur with infusion of large doses of AHF/VWF complex (human).

Rapid administration of a FVIII concentrate may result in vasomotor reactions.

Because ALPHANATE is made from human plasma, it may carry a risk of transmitting infectious agents, eg, viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent, despite steps designed to reduce this risk.

Monitor for development of FVIII and VWF inhibitors. Perform appropriate assays to determine if FVIII and/or VWF inhibitor(s) are present if bleeding is not controlled with expected dose of ALPHANATE.

The most frequent adverse drug reactions reported with ALPHANATE in >1% of infusions were pruritus, headache, back pain, paresthesia, respiratory distress, facial edema, pain, rash, and chills.

Please see full Prescribing Information for ALPHANATE at www.alphanate.com.

Reference: 1. ALPHANATE® (antihemophilic factor/von Willebrand factor complex [human]) Prescribing Information. Grifols.

GRIFOLS

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