Alphanate®

antihemophilic factor/von Willebrand factor complex (human)

Properties of factor-replacement treatment options for hemophilia A and von Willebrand disease (VWD)

ALPHANATE provides proven natural protection with the FVIII/VWF complex, with a large variety of dosing options to individualize each patient's therapy

Five convenient vial sizes with low reconstitution volume[1]

FVIII Potency	VWF Potency	Diluent size
250 IU FVIII range	250 IU VWF range	5 mL
500 IU FVIII range	500 IU VWF range	5 mL
1000 IU FVIII range	1000 IU VWF range	10 mL
1500 IU FVIII range	1500 IU VWF range	10 mL
2000 IU FVIII range	2000 IU VWF range	10 mL

-ALPHANATE can be administered at up to 10 mL/min

ALPHANATE packaging is designed for the unique needs of your high-volume patients.

GRIFOLS

Please see Important Safety Information on back and accompanying full Prescribing Information for ALPHANATE.

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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 adult 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, and perioperative management of bleeding 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	Indicated in adolescents and adults with hemophilia A for: routine prophylaxis to reduce the frequency of bleeding episodes; on-demand treatment, and control of bleeding episodes	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	19.1-22.6
Initial License date	1978	1986	2009	2015
VWF:RCo/FVIII ratio	1:1	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 600 IU VWF:RCo and 250 IU FVIII; 10 mL for 1200 IU VWF:RCo and 500 IU FVIII; 15 mL for 2400 IU VWF:RCo and 1000 IU FVIII	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 purification
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 325, 650, 1300, 1950, 2600 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. Do not use beyond expiration date
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.

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HEMOPHILIA A THERAPIES

PLASMA-DERIVED FACTOR VIII

BRAND NAME	ALPHANATE	Humate-P®	Hemofil® M	Koate®	Wilate®
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)	von Willebrand Factor/ Coagulation Factor VIII Complex (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 routine prophylaxis to reduce the frequency of bleeding episodes and for on-demand treatment and control of bleeding episodes in adolescents and adults with hemophilia A
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 adult 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	Indicated in children and adults with von Willebrand disease for on-demand treatment and control of bleeding episodes and for perioperative management of bleeding.
Half-life (hours)	17.9	12.2	14.8	16.1	19.6
Initial license date	1978	1986	1988	1974	2009
Type of plasma derived	FVIII/VWF	FVIII/VWF	FVIII	FVIII	FVIII/VWF
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	5 mL for 500 IU FVIII; 10 mL for 1000 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	Infuse intravenously at a rate comfortable to the patient, up to 10 mL/min	Inject intravenously at a slow speed of 2-4 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	Immunoaffinity chromatography, ion-exchange chromatography, solvent/detergent, nanofiltration	Solvent-detergent, heat treatment, PEG precipitation/depth filtration	Solvent/detergent, dry heat treatment, ion-exchange chromatography
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	250, 500, 1000, 1700 IU FVIII	250, 500, 1000 IU FVIII	500, 1000 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 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
Manufacturer	Grifols	CSL Behring	Shire	Grifols	Octapharma

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HEMOPHILIA A THERAPIES

		RECOMBINANT FACTOR VIII						
BRAND NAME	**Advate®**	**Adynovate®**	**Afstyla®**	**Eloctate®**	**Jivi®**	**Kovaltry®**	**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), PEGylated-aucl	Antihemophilic Factor (Recombinant)	Antihemophilic Factor (Recombinant)	Antihemophilic Factor (Recombinant)
Hemophilia A indication	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	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	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	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	In previously treated adults and adolescents 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	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	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	In children and adults with hemophilia A for: on-demand treatment and control 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	17.9 in adults and adolescents	14.2-14.3 in adults; 11.7-14.3 in adolescents; 12.0-12.1 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
Initial license date	2003	2015	2016	2014	2018	2016	2015	2008
Reconstitution volume	2 mL for 250, 500, 1000, 1500 IU FVIII; 5 mL for 2000, 3000, 4000 IU FVIII	2 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 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 5000, 6000 IU FVIII	2.5 mL for 500, 1000, 2000, and 3000 IU FVIII	2.5 mL for 250, 500, 1000 IU FVIII; 5 mL for 2000, 3000 IU FVIII	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	Infuse intravenously over a period of 1 to 15 min; maximum infusion rate 2.5 mL/min	Administer intravenously over a period of 1 to 15 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	Controlled multi-step process including two virus reduction steps complementing each other in their mode of action	Detergent; nanofiltration (15 nm)	Chromatography; nanofiltration (20 nm)	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	500, 1000, 2000, 3000	250, 500, 1000, 2000, 3000	250, 500, 1000, 2000, 2500, 3000, 4000	250, 500, 1000, 2000, 3000
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 24 months; do not freeze. May store at a maximum room temperature of 77°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 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. Do not return to refrigerator after room temperature storage
Manufacturer	Shire	Shire	CSL Behring	Bioverativ	Bayer	Bayer	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 2 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 severe 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 accompanying full Prescribing Information for ALPHANATE.

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

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