Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

University of Colorado Hemophilia & Thrombosis Center Pharmacy: FACTOR VIII CONCENTRATES W/VWF COMPLEX & RECOMBINANT VWF DOSING RECOMMENDATIONS

DOSING RECOMMENDATIONS FOR FACTOR VIII CONCENTRATES W/VWF COMPLEX & RECOMBINANT VWF CONCENTRATES

NOTE: Although dose can be estimated using the published guidelines, it is highly recommended that whenever possible, appropriate laboratory tests should be performed on the patient's plasma at suitable intervals to assure that adequate VWF: RCo and FVIII activity levels have been reached and are maintained. Individual dosage is based on the patient's weight, type and severity of hemorrhage, FVIII and VWF levels, presence of inhibitors and the recommendations of the treating physician.

Dosage and duration of treatment is dependent on the factor VIII and VWF: RCo deficiency, the location of the bleed, the patient's clinical condition and the recommendation of the treating physician. In cases of major surgery or life-threatening bleeding episodes, cautious replacement of factor is critical.

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	ALPHANATE-SD®	HUMATE-P™	WILATE®	VONVENDI™
MANUFACTURER	GRIFOLS	CSL BEHRING	OCTAPHARMA	SHIRE (formerly BAXALTA)
US LICENSURE DATE	1997 for hemophilia A; 2007 for VWD	1986 for hemophilia A; 1999 for VWD	2009	2015
RATIO Of Ristocetin Co-Factor units to FVIII units	1.33± 0.26:1 (The ratio of VWF: RCo to FVIII varies by lot, check the IU VWF:RCo/Vial to ensure accurate dosing)	2.4: 1	1.0:1.0	Contains only Ristocetin CoFactor Does NOT contain FVIII
CELL LINE; SOURCE MATERIAL	Pooled human plasma	Pooled human plasma	Pooled human plasma	Recombinant, Chinese Hamster Ovary (CHO)
PROTEIN PURIFICATION METHOD	-Cryoprecipitation -PEG precipitation -Affinity chromatography -Salt/glycine precipitation	-Cyroprecipitation -Al(OH)3 adsorption -Glycine precipitation -NaCl precipitation -Column Fractionation	-Cyroprecipitation -Ultra- and diafiltration -Sterile filtration -Ion exchange chromatography	-Ion exchange chromatography
VIRAL INACTIVATION METHODS	-Solvent/Detergent -Dry heat cycle	Pasteurization	-Solvent/ Detergent -Dry heat treatment	Solvent/Detergent
STABILIZING AGENTS	Albumin (human)	Albumin (human)	Albumin (human)	Mannitol, trehalose-dihydrate
INACTIVE INGREDIENTS	Albumin, arginine, histidine	Glycine, sodium citrate, NaCl, albumin	Glycine, sucrose, NaCl, sodium citrate, calcium chloride, polysorbate-80	Tri-sodium citra-dihydrate, glycine, mannitol, trehalose-dihydrate, polysorbate-80
SPECIFIC ACTIVITY (amount of clotting activity per weight of substance) of FVIII	5 units FVIII/mg of total protein, final product	1-2 units FVIII/mg of protein , final product	Not less than 60 units VWF:RCco and Not less than 60 units FVIII/mg of total protein.	123 ±24 units VWF:RCo/mg
MEAN HALF LIFE	17.9 ± 9.6 hours	~12.2 hours	19.6 ± 6.9 hours	21.9 ± 8.36 hours
BOX CONTENTS	Diluent: Sterile Water for Injection-5 mL (250 IU,500 IU), 10 mL (1000 IU, 1500 IU, 2000 IU); Mix2Vial™ filter transfer set	Diluent: Sterile Water for Injection-5 mL (600 risto), 10 mL (1200 risto),15 mL (2400 risto); Mix2Vial™ filter transfer set, alcohol swabs	Diluent: Sterile Water for Injection with 0.1% polysorbate-80 -5 mL (500 IU), 10 mL (1000 IU); Mix2vial™ transfer device; 10 mL syringe; infusion set; two alcohol swabs	Diluent: Sterile Water for Injection- 5mL (650 risto), 10mL (1300 risto), Mix2Vial™ filter transfer set
ASSAYS AVAILABLE	250 IU, 500 IU, 1000 IU, 1500 IU, 2000 IU	600 IUiu VWF:RCco/250 IU FVIII; 1200 IU VWF:RCco/500 IU FVIII; 2400 IU VWF:RCco/1000 IU FVIII	500 IU, 1000 IU	650 IU, 1300 IU

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INFUSION RATE	≤10 mL/minute Infuse within 3 hours of reconstitution.	4mL/minute Infuse within 3 hours of reconstitution.	2-4 mL/minute Infuse immediately after reconstitution.	4mL/minute Infuse within 3 hours of reconstitution. If infusing with rFVIII, infuse rFVIII within 10 minutes of infusing VONVENDI. No more than two (2) vials may be pooled into one syringe for administration. Only use plastic syringes for administration.
STORAGE REQUIREMENTS	▫Refrigerate or store at room temperature up to expiration date ≤77°F (25°C). ▫Do not freeze.	▫Refrigerate or store at room temperature up to expiration date ≤77°F (25°C). ▫Do not freeze.	▫Refrigerate 36°F to 46°F (2 to 8°C) to expiration date or store at room temp < 77 °F (25°C) for up to 6 months. ▫Once stored at room temperature, the product must not be returned to the refrigerator. ▫Do not freeze.	▫ Refrigerate 36°F to 46°F (2 to 8°C) to expiration date or store at room temp < 86 °F (30°C) for up to 12 months. ▫ Once stored at room temperature, the product must not be returned to the refrigerator. ▫Do not freeze. ▫Store vial in original box and protect from light.
DOSING GUIDELINES	**SEE PI FOR DOSING GUIDELINES FOR VWD PATIENTS' SURGICAL PROCEDURE RECOMMENDATIONS**	**Treatment of episodic bleeding in VWD**: 40-80 IU VWF: RCo/kg every 8-12 hours. • Adjust the dose according to the severity of the bleed and severity of the VWD	**Treatment of episodic bleeding in VWD:** **Minor Hemorrhages**: 20-40 IU/kg loading dose followed by and every 20-30 IU VWF: RCo/kg every 12-24 hours. Therapeutic Goal: VWF:RCo and FVIII activity trough levels of >30% **Major Hemorrhages**: 40-60 IU VWF: RCo/kg loading dose; then 20-40 IU/kg every 12-24 hours. Therapeutic Goal VWF: RCo and FVIII activity trough levels of > 50%. • Adjust the dose according to the extent and location of bleed and the patient's clinical condition. • VWD type 3 patients may require higher doses	**Treatment of episodic bleeding in VWD:** **Minor (epistaxis, oral bleeding, menorrhagia):** 40-50 IU/kg every 8 to 24 hours as clinically necessary **Major (severe epistaxis, menorrhagia, GI bleeding, CNS trauma, hemarthrosis, or traumatic hemorrhage):** 50-80 IU/kg loading dose followed by 40-60 IU/kg every 8 to 24 hours for approximately 2-3 days as clinically required. ***Hemostasis cannot be ensured until FVIII coagulation activity (FVIII: C) has reached 0.4 IU/dL or 40% of normal activity. If below 40%, or is unknown, it is necessary to administer an approved rFVIII (non-von Willebrand factor containing) factor with first infusion of VONVENDI, in order to achieve a hemostatic plasma level of FVIII:C.** **SEE PI FOR ADDITIONAL DOSING GUIDELINES**

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FDA APPROVED INDICATION(S) **FOR PATIENTS WITH VON WILLEBRAND DISEASE** **ICD 10 CODE: D68**	Von Willebrand Disease in adults and children in whom DDAVP is either ineffective or contraindicated: ☑Perioperative management Prevention and control of bleeding in Hemophilia A adults: ☑Episodic bleeds ☑Perioperative management NOT INDICATED FOR PATIENTS WITH SEVERE VWD TYPE III UNDERGOING MAJOR SURGERY	Von Willebrand Disease in adults and children in whom DDAVP is either ineffective or contraindicated: ☑Episodic bleeds ☑Perioperative management Prevention and control of bleeding in Hemophilia A adults: ☑Episodic bleeds	Von Willebrand Disease in adults in whom the use of DDAVP is ineffective or contraindicated: ☑Episodic bleeds ☑Perioperative NOT INDICATED FOR FVIII DEFICIENCY	Von Willebrand Disease in adults: ☑Episodic bleeds
COMMENTS	**Labeled in FVIII FIRST, then Ristocetin Cofactor units.** **DOSED IN FVIII**	**Labeled in Ristocetin Cofactor FIRST, then FVIII.** **DOSED IN RISTOCETIN COFACTOR**	**Labeled in Ristocetin CoFactor Cofactor FIRST, then FVIII.** **DOSED IN RISTOCETIN COFACTOR**	**Labeled in Ristocetin CoFactor units.**

Note: Recombinant products may be the ONLY products of choice for members of the Jehovah's Witnesses faith.

University of Colorado Hemophilia & Thrombosis Center Pharmacy
MEDICATION CHART DISCLAIMER

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Disclaimer: Information regarding factor products has been derived from the manufacturer FDA-approved Prescribing Information sheets and other sources and compiled by the staff at the Hemophilia & Thrombosis Center Pharmacy at the University of Colorado. Although every effort is made to assure accuracy, the information was not reviewed by the manufacturer of any particular drug. Information has been provided only as an easily accessible reference of basic information. This information is provided as is without any guarantees or warranty. Dosing information is not intended to replace a physician's judgment on the appropriate dosing regimen for each individual patient.