Hemophilia and Thrombosis Center

UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

HTC Pharmacy

Bleeding Disorder Product Comparison Chart

2019

303-724-0168 /1-888-724-7427
medschool.ucdenver.edu/htc

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

University of Colorado Hemophilia & Thrombosis Center Pharmacy: RECOMBINANT FACTOR VIII PRODUCTS DOSING RECOMMENDATIONS

FULL STANDARD DOSING RECOMMENDATIONS

Dosage and frequency of treatment is dependent on the level of factor VIII deficiency, the location and severity of the bleed, and the patient's individual clinical response. Patients may vary in their pharmacokinetic response (e.g., half-life, in vivo recovery) and clinical response to factor products.

One unit per kilogram body weight will raise the Factor VIII level by 2% international units per deciliter [IU/dL].

Dosage can be estimated using these standard equations:

Desired Increment in Factor VIII concentration (IU/dL or % of normal) = [Total Dose (IU) / body weight (kg)] x 2 (IU/dL per IU/kg)

OR

Required Dose (IU) = body weight (kg) x desired factor VIII Rise (IU/dL or % of normal) x 0.5 (IU/kg per IU/dL)

Dosing examples for standard recombinant Factor VIII products:

Adult Prophylaxis: 20-40 units/kg every other day or three times per week
Children <12 yo Prophylaxis: 25-50 units/kg every other day or three times per week
Minor muscle or oral bleed: 10-30 units/kg every 12-24 hours until bleeding resolution is achieved
Major muscle or joint bleed: 30-50 units/kg every 8-24 hours until bleeding resolution is achieved

University of Colorado Hemophilia & Thrombosis Center Pharmacy: RECOMBINANT FACTOR VIII PRODUCTS CHART 1 of 2

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

	RECOMBINATE™	KOGENATE®FS	ADVATE™	XYNTHA®
MANUFACTURER	SHIRE (formerly BAXALTA)	BAYER	SHIRE (formerly BAXALTA)	PFIZER
US LICENSURE DATE	1992	1993	2003	2008
GENERATION OF PRODUCT (see definition below)	First Generation[1]	Second Generation[2]	Third Generation[3]	Third Generation[3] (B-Domain deleted)
CELL LINE FORMULATION, SOURCE MATERIAL	Chinese Hamster Ovary (CHO) cell line	Baby hamster kidney (BHK) cell line	Chinese Hamster Ovary (CHO) cell line	Chinese Hamster Ovary (CHO) cell line
PROTEIN PURIFICATION METHOD	-Monoclonal antibody immunoaffinity chromatography	-Ion exchange chromatography -Monoclonal antibody immunoaffinity chromatography	-Monoclonal antibody immunoaffinity chromatography	-Affinity chromatography using patented synthetic peptide affinity ligand
VIRAL INACTIVATION METHOD	Micro-Filtration; Ion exchange chromatography as shown in model virus studies	Solvent/Detergent	Solvent/Detergent	Solvent/Detergent; virus retaining nanofiltration
ALBUMIN USED IN MANUFACTURING PROCESS	Yes (Human)	Yes (Human)	No	No
STABILIZING AGENTS	Albumin	Sucrose	Trehalose, Mannitol	Sucrose
INACTIVE INGREDIENTS	Albumin (human), Ca, PEG 3350, NaCl, histidine, Polysorbate-80	Sucrose, glycine, histidine, sodium, calcium, chloride, polysorbate- 80, imidazole, tri-n-butyl phosphate, copper	Mannitol, trehalose, sodium chloride, histidine, tris, calcium chloride, polysorbate-80 and/or glutathione	NaCl, Sucrose, histidine, CaCl, polysorbate-80
SPECIFIC ACTIVITY (amount of clotting activity per weight of substance)	4,000-8,000 IU/mg of protein	~4,000 IU/mg of protein	4,000-10,000 IU/mg of protein	5,500-9,000 IU/mg of protein
MEAN HALF LIFE	14.6 ± 4.9 hrs	**Pediatric:**(4.4-18.10 yo): 10.7 hrs (mean range 7.8-15.3 hrs) **Adult (>18 yo):** 14.07 ± 2.62 hrs	**Pediatric:**1-24 mo: 8.7 ± 1.4 hrs 2-5 yo: 9.5 ± 1.8 hrs 5-12 yo: 11.2 ± 3.5 hrs 12-16 yo**:** 12.0 ± 2.9 hrs **Adult(>16 yo):** 12.0 ± 4.2 hrs	**Pediatric:**(3.7-5.8 yo): 8.3 ±2.7 hrs (14-15 yo): 6.9 ± 2.4 hrs **Adult (12-60 yo)**: 11.2 ± 6.2 hrs

1. First generation: human or animal albumin used as both nutrients in cell culture and as stabilizer in final product
2. Second generation: human albumin used as nutrient in cell culture, but not as stabilizer in final product
3. Third generation: no human or animal albumin used either as nutrient in cell culture or as stabilizer in final product

NOTE: Recombinant technology may be the ONLY product of choice for patients of the Jehovah's Witnesses faith.

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

University of Colorado Hemophilia & Thrombosis Center Pharmacy: RECOMBINANT FACTOR VIII PRODUCTS CHART 1 of 2

	RECOMBINATE™	KOGENATE®FS	ADVATE™	XYNTHA®
BOX CONTENTS	Diluent: 5 mL (all sizes) Sterile water, Baxject™ II Needleless Transfer Device	Diluent: Sterile water 2.5 mL (250, 500, 1000), 5 mL (2000, 3000) vial adapter with 15 micrometer filter, infusion set	Diluent: 2 mL (250, 500, 1000, 1500), 5 mL (2000, 3000, 4000) Sterile water, Baxject™ III Needleless Transfer Device 2mL kits also contain microbore butterfly	Diluent: 4 mL sodium chloride prefilled syringe with plunger rod, vial adapter, 23G infusion set, alcohol pads, bandage, gauze SOLOFUSE: Prefilled dual-chamber syringe with lyophilized Xyntha® powder in one chamber and sodium chloride in other chamber, 23G infusion set, alcohol pads, bandage, gauze
ASSAYS AVAILABLE	250 IU, 500 IU, 1000 IU, 1500 IU, 2000 IU	250 IU,500 IU,1000 IU, 2000 IU, 3000 IU	250 IU, 500 IU,1000 IU,1500 IU, 2000 IU, 3000 IU, 4000 IU	250 IU, 500 IU, 1000 IU, 2000 IU, 3000 IU (Solofuse only)
INFUSION RATE	Infuse at a rate of ≤5 mL/minute (maximum: 5 mL/minute) Infuse within 3 hours of reconstitution.	Infuse over 1 to 15 minutes (based on patient tolerability) Infuse within 3 hours of reconstitution.	Infuse over ≤5 minutes (maximum: 10 mL/minute) Infuse within 3 hours of reconstitution.	Infuse over several minutes; adjust based on patient comfort. Do not admix or administer in same tubing as other medications. Infuse within 3 hours of reconstitution.
STORAGE REQUIREMENTS	☑Room temperature <86°F until expiration date. ☑Do not freeze. ☑ Keep the vial in the original carton and protect from light.	☑Refrigerate (36°F to 46°F) to expiration date. ☑ Room temp < 77 °F for up to 12 months. ☑Do not freeze. ☑Once product is stored at room temperature product it should not be returned to refrigerator. ☑ Keep the vial in the original carton and protect from light.	☑Refrigerate (36°F to 46°F) to expiration date. ☑Room temp < 86 °F for up to 6 months. ☑Do not freeze. ☑Once product is stored at room temperature it should not be returned to refrigerator. ☑ Keep the vial in the original carton and protect from light.	☑Refrigerate (36°F to 46°F) to expiration date. ☑Room temp < 77 °F for up to 3 months. ☑ Do not freeze. ☑Once product is stored at room temperature it should not be returned to refrigerator. ☑ Keep the vial in the original carton and protect from light.
DOSING GUIDELINES	SEE BELOW	SEE BELOW	SEE BELOW	SEE BELOW
FDA APPROVED INDICATION **FOR PATIENTS WITH HEMOPHILIA A OR FACTOR VIII DEFICIENCY ONLY** **ICD-10 DIAGNOSIS CODE D66**	Prevention and control of bleeding in adults and children: ☑ episodic bleeds ☑ perioperative management **NOT INDICATED FOR VON WILLEBRAND DISEASE**	Prevention and control of bleeding in adults and children: ☑ episodic bleeds ☑ perioperative management ☑ routine prophylaxis **NOT INDICATED FOR VON WILLEBRAND DISEASE**	Prevention and control of bleeding in adults and children: ☑ episodic bleeds ☑ perioperative management ☑ routine prophylaxis **NOT INDICATED FOR VON WILLEBRAND DISEASE**	Prevention and control of bleeding in adults and children: ☑ episodic bleeds ☑ surgical prophylaxis **NOT INDICATED FOR VON WILLEBRAND DISEASE**
COMMENTS			2 mL vials should be infused with butterfly provided to prevent factor loss due to high concentration.	

University of Colorado Hemophilia & Thrombosis Center Pharmacy: RECOMBINANT FACTOR VIII PRODUCTS CHART 2 of 2

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

	NOVOEIGHT®	KOLVATRY®	NUWIQ®	AFSTYLA ®
MANUFACTURER	NOVO NORDISK	BAYER	OCTAPHARMA	CSL Behring
US LICENSURE DATE	2013	2016	2015	2016
GENERATION OF PRODUCT (see definition below)	Third generation[3] (B-Domain replaced with 21 amino acid linker)	Third Generation[3]	Third generation[3] (B-Domain Deleted)	Third generation[3], single-chain B-domain deleted rFVIII
CELL LINE FORMULATION, SOURCE MATERIAL	Chinese Hamster Ovary (CHO) cell line	Baby hamster kidney (BHK) cell line	Human Embryonic Kidney (HEK) cell line	Chinese Hamster Ovary (CHO)
PROTEIN PURIFICATION METHOD	-Ion exchange chromatography antibody - Immunoaffinity chromatography	-Chromatography -Filtration	Chromatography	N/A
VIRAL INACTIVATION METHOD	Solvent/Detergent; 20-nm and gel filtration	Solvent/Detergent; 20-nm nanofiltration	Solvent/Detergent 20-nm nanofiltration	Solvent/Detergent 20 nm nanofiltration
ALBUMIN USED IN MANUFACTURING PROCESS	No	No	No	No
STABILIZING AGENTS	Sucrose	Sucrose	Sucrose	Sucrose
INACTIVE INGREDIENTS	NaCl, L-histidine, sucrose, polysorbate-80, L-methionine, calcium chloride	Glycine, sucrose, sodium chloride, calcium chloride, histidine, polysorbate-80	NaCl, sucrose, L-arginine HCl, calcium chloride dihydrate, poloxamer 188, sodium citrate dihydrate	L-histidine, polysorbate-80, calcium chloride, sodium chloride, sucrose
SPECIFIC ACTIVITY (amount of clotting activity per weight of substance)	~8340 IU/mg of protein	~4000 IU/mg of protein	~8124 IU/mg of protein	8200-16000 IU/mg
MEAN HALF LIFE	**Pediatric:**0 to <6 yo: 7.7 ± 1.8 hrs 6 to <12 yo: 10.0 ± 1.7 hrs **Adult (>12 yo):** 10.8 ± 4.9 hrs	**Pediatric:** (12-17 yo): 11.7±1.11 hrs **Adult (>12yo):** 14.3 ± 3.7 hrs	**Pediatric:** 2 to 5 yo: 11.9 ± 5.4 hrs 6 to <12 yo: 13.1 ± 2.6 hrs **Adult (>12yo):** 17.1 ± 11.2 hrs	**Chromogenic Assay** **Pediatric (0-6 yo):** 10.4 hrs. **(6-12 yo):** 10.2 hrs. **Adolescents (12-18 yo**): 14.3 hrs. **Adults (>18 yo):** 14.2 hrs.
BOX CONTENTS	Diluent: 4ml sodium chloride prefilled syringe, vial adapter w/25 micrometer filter	Diluent: Sterile water prefilled syringe: 2.5 mL (250, 500, 1000), 5 mL (2000, 3000, vial adapter with 15 micrometer filter, infusion set	Diluent: 2.5ml (all sizes) Sterile water for Injection prefilled syringe, vial adapter, butterfly needle and two alcohol swabs.	Diluent: Sterile water for Injections 2.5 mL (250, 500, 1000), 5ml (1500, 2000, 2500, 3000), Mix2Vial filter transfer set, alcohol swab

University of Colorado Hemophilia & Thrombosis Center Pharmacy:
RECOMBINANT FACTOR VIII PRODUCTS CHART 2 of 2

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

	NOVOEIGHT®	KOLVATRY®	NUWIQ®	AFSTYLA ®
ASSAYS AVAILABLE	250 IU, 500 IU, 1000 IU, 1500 IU, 2000 IU, 3000 IU	250 IU, 500 IU, 1000 IU, 2000 IU,3000 IU	250 IU, 500 IU, 1000 IU, 2000 IU	250 IU, 500 IU, 1000 IU, 1500 IU, 2000 IU, 2500 IU, 3000 IU
INFUSION RATE	Infuse over 2 to 5 minutes Infuse within 4 hours of reconstitution.	Infuse over 1 to 15 minutes (based on patient tolerability) Infuse within 3 hours of reconstitution.	Infuse at maximum rate of 4ml per minute, adjust based on patient comfort. Infuse within 3 hours of reconstitution.	Infuse at maximum rate of 10 mL per minute (determined by patient comfort level) Infuse within 4 hours of reconstitution.
STORAGE REQUIREMENTS	☑Refrigerate (36°F to 46°F) to expiration date. ☑ Room temp < 86 °F for up to 12 months. ☑Do not freeze. ☑Once product is stored at room temperature it should not be returned to refrigerator. ☑ Keep the vial in the original carton and protect from light.	☑Refrigerate (36°F to 46°F) to expiration date. ☑ Room temperature <77°F for up to 3 months. ☑Do not freeze. ☑Once product is stored at room temperature it should not be returned to refrigerator. ☑ Keep the vial in the original carton and protect from light.	☑Refrigerate (36°F to 46°F) to expiration date. ☑ Room temperature <77°F for up to 3 months. ☑ Do not freeze. ☑ Once product is stored at room temperature it should not be returned to refrigerator. ☑ Keep the vial in the original carton and protect from light.	☑Refrigerate (36°F to 46°F) to expiration date. ☑ Room temp < 77 °F for up to 3 months. ☑ Do not freeze. ☑ Once product is stored at room temperature product it should not be returned to refrigerator. ☑ Keep the vial in the original carton and protect from light.
DOSING GUIDELINES	**Children ≤ 12 yo:** 25-60 IU/kg 3 times weekly or 25-50 IU/kg every other day **Adults ≥ 12 yo**: 25-50 IU/kg three times a week or 20-40 IU/kg every other day	**Children ≤ 12 yo:** 25-50 IU/kg 2 times, per week, 3 times per week or every other day **Adults/adolescents:** 20-40 IU/kg 2 or 3 times per week	Prophylaxis: **Children 2-11yo**: 30-50 IU/kg every other day **Adolescents 12-17 yo:** 30-40 IU/kg every other day	**Children<12 yo prophylaxis:** 30-50 IU/kg/dose 2 to 3 times per week. More frequent or higher doses may be required in this age group. **Adults and adolescents prophylaxis:** 20-50 IU/kg/dose 2 to 3 times per week.
FDA APPROVED INDICATION **FOR PATIENTS WITH HEMOPHILIA A OR FACTOR VIII DEFICIENCY ONLY ICD-10 DIAGNOSIS CODE D66**	Prevention and control of bleeding in adults and children: ☑ episodic bleeds ☑ perioperative management ☑ routine prophylaxis **NOT INDICATED FOR VON WILLEBRAND DISEASE**	Prevention and control of bleeding in adults and children: ☑ episodic bleeds ☑ perioperative management ☑ routine prophylaxis **NOT INDICATED FOR VON WILLEBRAND DISEASE**	Prevention and control of bleeding in adults and children: ☑ episodic bleeds ☑ perioperative management ☑ routine prophylaxis **NOT INDICATED FOR VON WILLEBRAND DISEASE**	Prevention and control of bleeding in adults and children: ☑ episodic bleeds ☑ perioperative management ☑ routine prophylaxis **NOT INDICATED FOR VON WILLEBRAND DISEASE**
COMMENTS		Due to narrow internal tip diameter of glass syringe, IV systems and port adaptors containing an internal spike are known to have incompatibility issues. Attach an appropriately sized plastic syringe that is compatible with port adaptor or other connector to administer.		If the one-stage clotting assay is used, multiply the result by a conversion factor of 2 to determine the patient's FVIII activity level.

1. First generation: human or animal albumin used as both nutrients in cell culture and as stabilizer in final product
2. Second generation: human albumin used as nutrient in cell culture, but not as stabilizer in final product
3. Third generation: no human or animal albumin used either as nutrient in cell culture or as stabilizer in final product

NOTE: Recombinant technology may be the ONLY product of choice for patients of the Jehovah's Witnesses faith.

University of Colorado Hemophilia & Thrombosis Center Pharmacy: RECOMBINANT FACTOR VIII CONCENTRATES EXTENDED HALF-LIFE

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

	ELOCTATE®	ADYNOVATE™	JIVI®
MANUFACTURER	BIOVERATIV (FORMERLY BIOGEN IDEC)	SHIRE (FORMERLY BAXTER)	BAYER
US LICENSURE DATE	2014	2015	2018
GENERATION OF PRODUCT (see definition below)	Third generation[1] (Fc Fusion Protein (B-Domain deleted)	Third generation (Pegylated)	Third generation B-Domain deleted (Peglated)
CELL LINE FORMULATION, SOURCE MATERIAL	Human embryonic kidney (HEK) cell line	Chinese Hamster Ovary (CHO) cell line	Baby Hamster Kidney (BHK) cell line
PROTEIN PURIFICATION METHOD	Affinity chromatography	Monoclonal antibody immunoaffinity chromatography	Chromatography and ultrafiltration
VIRAL INACTIVATION METHOD	Detergent and filtration	Solvent/Detergent	Detergent and filtration
ALBUMIN USED IN MANUFACTURING PROCESS	No	No	No
STABILIZING AGENTS	Sucrose	Mannitol	Sucrose
INACTIVE INGREDIENTS	Sucrose, NaCl, L-histidine, calcium chloride, polysorbate-20	Tris (hydroxymethyl) aminomethane, calcium chloride, mannitol, sodium chloride, trehalose dihydrate, glutathione, histidine, polysorbate -80	Glycine, sucrose, histidine, sodium chloride, calcium chloride, polysorbate-80
SPECIFIC ACTIVITY (amount of clotting activity per weight of substance)	4,000-10,000 IU/mg of protein	2700-8000 IU/mg protein	10,000 IU/mg of protein
MEAN HALF LIFE	**Pediatrics:** 1-5 yo: 12.7 hours 6-11 yo: 14.9 hours 12-17 yo: 16.4 hours **Adults (>18 yo):** 19.7 hours	**Pediatric:** <6 yo: 11.8 ± 2.43 hours 6-<12 yo: 12.4 ± 1.67 hours 12-18 yo: 13.43 ± 4.05 hours **Adults (>18yo)** : 14.69 ± 3.79 hours	**Adults (>12 yo):** 17.9 ± 4.0 hours (chromogenic) 17.4 ± 3.8 hours (one-stage assay)
Ratio of the mean half-life of long-acting factor/rFVIII	1.5	1.4	1.4
BOX CONTENTS	Diluent: 3 mL Sterile Water for Injection prefilled syringe, vial adapter	Diluent: 2 mL (250, 500, 1000 IU), 5mL (2000 IU) Sterile Water for injection , BAXJECT III Hi-flow transfer device	Diluent: 2.5 mL Sterile Water for Injection prefilled syringe, vial adapter w/filter, 25G butterfly needle
ASSAYS AVAILABLE	250 IU, 500 IU, 750 IU, 1000 IU, 1500 IU, 2000 IU, 3000 IU, 4000 IU, 5000 IU, 6000 IU	250 IU, 500IU, 1000 IU, 2000 IU	500 IU, 1000 IU, 2000 IU, 3000 IU
INFUSION RATE	Infuse at a rate of ≤10 mL/minute (maximum: 10 mL/minute) Infuse within 3 hours of reconstitution.	Infuse at a rate of ≤ 5 minutes (maximum: 10 mL/minute) Infuse within 3 hours of reconstitution.	Infuse at a rate of 1-15 minutes (maximum: 2.5 mL/minute) Infuse within 3 hours of reconstitution.

University of Colorado Hemophilia & Thrombosis Center Pharmacy: RECOMBINANT FACTOR VIII CONCENTRATES EXTENDED HALF-LIFE

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

	ELOCTATE®	ADYNOVATE™	JIVI®
STORAGE REQUIREMENTS	▫Refrigerate (36°F to 46°F) to expiration date or store at room temp < 86 °F for up to 6 months ▫Do not freeze ▫ Once stored at room temperature, do not return the product to the refrigerator ▫Store vial in original box and protect from light	▫Refrigerate (36°F to 46°F) to expiration date or store at room temp < 86 °F for up to 3 months ▫Do not freeze ▫ Once stored at room temperature, do not return the product to the refrigerator ▫ Store vial in original box and protect from light	▫Refrigerate (36°F to 46°F) to expiration date or store at room temp < 77 °F for up to 6 months ▫Do not freeze ▫ Once stored at room temperature, do not return the product to the refrigerator ▫ Store vial in original box and protect from light
DOSING GUIDELINES	Prophylaxis: **Children < 6yo**: Starting regimen 50 IU/kg twice a weekly. Adjust dose based on patient response with dosing range of 25-65 IU/kg every 3-5 days. More frequent or higher doses of up to 80 IU/kg may be required. **Adults/children > 6yo:** 50 units/kg every 4 days or 25-65 units/kg every 3-5 days. SEE PRESCRIBING INFORMATION FOR OTHER REGIMENS	Prophylaxis: **Children < 12 yo**: 55 units/kg twice a week (with max dose of 70 units/kg). Adjust dose based on the patient's clinical response. **Adults/children >12 yo:** 40-50 units/kg twice a week. Adjust dose based on the patient's clinical response. SEE PRESCRIBIING INFORMATION FOR OTHER REGIMENS.	Prophylaxis: **Adults/children >12 yo:** 30-40 units/kg twice weekly Based on the bleeding episodes the regime may be adjusted to 45-60 units/kg every 5 days. A regime may be individually adjusted to less or more frequent dosing. The total recommended max dose per infusion is approximately 6000 IU. SEE PRESCRIBIING INFORMATION FOR OTHER REGIMENS.
FDA APPROVED INDICATION FOR PATIENTS WITH HEMOPHILIA A OR FACTOR VIII DEFICIENCY ONLY **ICD-10 DIAGNOSIS CODE D66** **NOT INDICATED FOR VON WILLEBRAND DISEASE**	Prevention and control of bleeding in adults and children: ☑ On-demand treatment ☑ Routine prophylaxis ☑ Perioperative management	Prevention and control of bleeding in adults and children: ☑ On-demand treatment ☑ Routine prophylaxis ☑ Perioperative management	Prevention and control of bleeding in adults: ☑ On-demand treatment ☑ Routine prophylaxis ☑ Perioperative management Not indicated for use in children <12 years old

1. Third generation rFVIII: : No human or animal albumin used either as nutrient in cell culture or as stabilizer in final product

NOTE: Recombinant technology may be the ONLY product of choice for patients of the Jehovah's Witnesses faith.

University of Colorado Hemophilia & Thrombosis Center Pharmacy:
PLASMA DERIVED FACTOR VIII CONCENTRATES

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

	ALPHANATE-SD®	KOATE-DVI®	MONOCLATE-P®	HEMOFIL-M™
MANUFACTURER	GRIFOLS	GRIFOLS FOR KEDRION	CSL BEHRING	SHIRE (formerly Baxalta)
US LISCENSURE DATE	1997 Hemophilia A; 2007 VWD	1986 Hemophilia A; 1999 VWD	1990	1988
PROTEIN PURIFICATION METHOD	-Cryoprecipitation -PEG precipitation -Affinity chromatography -Salt/glycine precipitation	-Fractionation -Gel Chromatography	-Monoclonal antibody immuneoaffinity chromatography	-Monoclonal antibody immunoaffinity chromatography -Ion exchange chromatography
VIRAL INACTIVATION METHOD	-Solvent/ Detergent -Dry Heat Cycle	-Solvent /Detergent -Dry Heat Cycle	-Pasteurization	-Nanofiltration -Solvent/Detergent
INACTIVE INGREDIENTS	Albumin (Human), arginine, histidine	PEG, glycine, polysorbate-80, tri-n-butyl phosphate, calcium, aluminum, histidine, Albumin	Calcium chloride, albumin, mannitol, histidine, pH is adjusted with hydrochloric acid and/or sodium hydroxide.	Albumin, PEG 3350, histidine, glycine, mouse protein, tri-n-butyl phosphate, octoxynol-9
SPECIFIC ACTIVITY (amount of clotting activity per weight of substance)	≥5 units FVIII/mg of protein, final product	9-22 units FVIII/mg of protein, final product	4-10 units FVIII/mg of protein, final product	2-22 units FVIII/mg protein, final product
MEAN HALF LIFE	17.9 ± 9.6 hours	~16.12 hours	~17.5 hours	14.8 ±3.0 hours
BOX CONTENTS	Diluent: 5 mL (250, 500), 10 mL (1000, 1500, 2000) Sterile Water for Injection, Mix2Vial filter transfer set	Diluent: 5 mL (250, 500), 10 mL (1000) Sterile Water for Injection; transfer needle, filter needle, winged infusion set	Diluent: 2.5 mL (250), 5 mL (500), 10 mL (1000, 2000) Sterile Water for Injection, transfer needle, vented filter spike, filter needle, winged infusion set, alcohol swabs	Diluent: 10 mL (all sizes) Sterile Water for Injection, transfer needle, filter needle
ASSAYS AVAILABLE	250 IU, 500 IU, 1000 IU, 1500 IU, 2000 IU	250 IU, 500 IU, 1000 IU	250 IU, 500 IU, 1000 IU, 1500 IU	250 IU, 500 IU, 1000 IU, 1700 IU
INFUSION RATE	≤10 mL/minute Use within 3 hours of reconstitution.	Full dose in 5-10 minutes Use within 3 hours of reconstitution.	At a comfortable rate (2mL/minute) Use within 3 hours of reconstitution.	Up to 10 mL/minute Use within 3 hours of reconstitution.

University of Colorado Hemophilia & Thrombosis Center Pharmacy: PLASMA DERIVED FACTOR VIII CONCENTRATES

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

	ALPHANATE-SD®	KOATE-DVI®	MONOCLATE-P®	HEMOFIL-M™
STORAGE REQUIREMENTS	▫Refrigerate or store at room temperature 25°C (≤ 77°F) up to expiration date. ▫Do not freeze.	▫Refrigerate 2°C to 8°C (36°F to 46°F) to expiration date ▫Store at room temp 25°C (< 77 °F)for up to 6 months. ▫Do not freeze.	▫Refrigerate 2°C to 8°C (36°F to 46°F) to expiration date. ▫Store at room temp 25°C (< 77 °F) for up to 6 months. ▫Do not freeze.	▫Refrigerate or at room temperature 30°C (≤86°F) until expiration date. ▫Do not freeze.
FDA APPROVED INDICATION **FOR PATIENTS WITH HEMOPHILIA A OR FACTOR VIII DEFICIENCY** **ICD-10 DIAGNOSIS CODE** **D66** **VON WILLEBRAND DISEASE** **ICD-10 DIAGNOSIS CODE** **D68**	Prevention and control of bleeding in Hemophilia A adults: Episodic bleeds Perioperative management Von Willebrands Disease in adults and children: ☑ Perioperative management in patients in whom DDAVP is either ineffective or contraindicated.	Prevention and control of bleeding in Hemophilia A adults: Episodic bleeds Perioperative management	Prevention and control of bleeding in Hemophilia A adults: Episodic bleeds Perioperative management	Prevention and control of bleeding in Hemophilia A adults: Episodic bleeds
DOSING GUIDELINES	SEE BELOW	SEE BELOW	SEE BELOW	SEE BELOW
COMMENTS	**NOT INDICATED FOR PATIENTS WITH SEVERE VON WILLEBRAND DISEASE TYPE III**	Koate-DVI contains naturally occurring VWF; **NOT INDICATED FOR THE TREATMENT OF VON WILLEBRAND DISEASE**	Contains reduced amounts of VWF:Ag Currently only available in 1000 IU & 1500 IU assay size; **NOT INDICATED FOR THE TREATMENT OF VON WILLEBRAND DISEASE**	

NOTE: Recombinant technology may be the ONLY product of choice for patients of the Jehovah's Witnesses faith.

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

University of Colorado Hemophilia & Thrombosis Center Pharmacy: FACTOR IX PRODUCTS DOSING RECOMMENDATIONS

STANDARD FIX DOSING RECOMMENDATIONS

Dosage and duration of treatment is dependent on the factor IX 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, careful control of replacement factor is critical. Patients may vary in their pharmacokinetic (e.g., half-life, in vivo recovery) and clinical response to factor products. Whenever possible, perform appropriate laboratory tests including serial factor IX activity assays.

One unit per kilogram body weight will raise the Factor IX level by 1% international units per deciliter [IU/dL].
Dosage can be estimated using these standard equations:

Required Dose (IU)=body weight (kg) x desired Factor IX increase (IU/dL or % of normal) **OR**
Desired Increment in Factor IX concentration (IU/dL or % of normal) = Total Dose (IU)/ body weight (kg)

Dosing examples for standard recombinant/plasma Factor IX dosing:

Adult prophylaxis: 40-60 units/kg twice a week
Children< 12 yo prophylaxis: 60-80 units/kg twice a week
Minor bleed: 40-50 units/kg every 12-24 hours until healing is achieved
Major or joint bleed: 80-100 units/kg every 8-24 hours until bleeding resolution is achieved
*Dosing is 15-20% higher for Benefix and Rixubis

University of Colorado Hemophilia & Thrombosis Center Pharmacy: FACTOR IX CONCENTRATES HIGH PURITY (RECOMBINANT AND HUMAN)

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

	BENEFIX-RT®	IXINITY®	RIXUBIS™	MONONINE®	ALPHANINE-SD®
MANUFACTURER	PFIZER	Aptevo BioTherapeutics LLC	SHIRE (formerly Baxter)	CSL BEHRING	GRIFOLS
US LICENSURE DATE	1997	2015	2013	1992	1996
CLASSIFICATION	RECOMBINANT	RECOMBINANT	RECOMBINANT	HUMAN, HIGH PURITY	HUMAN, HIGH PURITY
CELL LINE FORMULATION, SOURCE MATERIAL	Chinese hamster ovary (CHO) cells	Chinese hamster ovary (CHO) cells	Chinese hamster ovary (CHO) cells	Pooled human plasma	Pooled human plasma, albumin added as a stabilizer
PROTEIN PURIFICATION PROCESS	Chromatography	Solvent/detergent Chromatography	Chromatography	Monoclonal antibody immunoaffinity chromatography	Column chromatography
VIRAL INACTIVATION METHODS	Nano filtration	Solvent/detergent Nano filtration	Solvent/detergent 15nm filtration	Nano filtration Vapor heat	Solvent/detergent Nano filtration
STABILIZING AGENTS	Sucrose	Trehalose Dihydrate Mannitol	Sucrose	Albumin	Albumin
INACTIVE INGREDIENTS	Polysorbate-80, sucrose, glycine, L-histidine, NaCl	Histidine, mannitol, trehalose dihydrate, Sodium Chloride, polysorbate -80	L-histidine, Sodium Chloride, calcium chloride, mannitol, sucrose, polysorbate- 80	Histidine, NaCl, mannitol, polysorbate-80, hydrochloric acid and/or sodium hydroxide may have been used to adjust pH, albumin (human)	Albumin (human)
SPECIFIC ACTIVITY (amount of clotting activity per weight of substance)	Greater than or equal to 200 units/mg of protein	200-230 units/mg of protein	Greater than or equal to 200 units/mg of protein	Not less than 190 units/mg of protein	Not less than 150 Factor IX units/mg of protein, final product
MEAN HALF LIFE	**Pediatric:** 2-12 yo. : 19.8 ±4 hrs 12-15 yo.: 21.1±4.5hrs **Adults (>15 yo)** :18.1 ± 5.1 hrs	24 ±7 hrs	**Pediatric:** <6yrs: 27.7 ± 2.7 hrs. 6-11yrs: 23.2 ± 1.6 hrs. **Adult:** ≥12yrs: 25.7± 1.5 hrs.	~25.3 hours	~21 hours
BOX CONTENTS	Diluent: 0.234% sodium chloride 5mL prefilled syringe, vial adapter, 23G infusion set, alcohol swabs, bandage, gauze pad	Diluent: 5ml of Sterile Water for Injection with plunger rod attached, vial adapter with filter, and a sterile 20 ml LUER-LOK Administration syringe.	Diluent: 5mL Sterile Water for Injection, BAXJECT II transfer device	Diluent: Sterile Water for Injection 5mL = 500IU, 10mL=1000 IU, double-ended needle for reconstitution, vented filter spike for withdrawal, alcohol swabs, 25G winged infusion set	Diluent: 10 mL Sterile Water for Injection (all assays); Mix2Vial filter transfer set
ASSAYS AVAILABLE	250 IU,500 IU, 1000 IU, 2000 IU, 3000 IU	500 IU, 1000 IU, 1500 IU, 2000 IU, 3000 IU	250 IU,500 IU, 1000 IU, 2000 IU, 3000 IU	500 IU, 1000 IU	500 IU, 1000 IU, 1500 IU

University of Colorado Hemophilia & Thrombosis Center Pharmacy: FACTOR IX CONCENTRATES HIGH PURITY (RECOMBINANT AND HUMAN)

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

	BENEFIX-RT®	IXINITY®	RIXUBIS™	MONONINE®	ALPHANINE-SD®
INFUSION RATE	Over several minutes according to patient's comfort level Infuse within 3 hours after reconstitution.	≤10ml/minute Infuse within 3 hours after reconstitution.	10 mL/minute Infuse within 3 hours after reconstitution.	2ml/minute Infuse within 3 hours after reconstitution.	≤10ml/minute Infuse within 3 hours after reconstitution.
STORAGE REQUIREMENTS	▫Refrigerate 2 to 30 °C (36 to 86 °F) or store at room temperature ≤ 30 °C (86°F) until expiration date. ▫Do not freeze. ▫Keep the vial in the original carton and protect from light.	▫Store at 2 to 25 °C (36-77° F) or room temperature ≤ 25°C (77°F) ▫ Do not freeze. ▫ Once product is stored at room temperature it should not be returned to refrigerator. ▫ Keep the vial in the original carton and protect from light.	▫Refrigerate 2 to 8 °C (36 to 46°F) or room temperature not to exceed 30 °C (86°F) for up to 36 months. ▫ Do not freeze. ▫ Once product is stored at room temperature it should not be returned to refrigerator. ▫ Keep the vial in the original carton and protect from light.	▫Refrigerate 2 to 8 °C (36 to 46 °F) up to the expiration printed on label ▫May store at room temperature < 25°C (77 °F) for up to 1 month. ▫ Do not freeze. ▫ Keep the vial in the original carton and protect from light.	▫Refrigerate 2 to 8 °C (36 to 46 °F) up to the expiration printed on label. ▫May be stored at room temperature not to exceed 30°C (≤ 86°F) for up to 1 month ▫ Do not freeze. ▫ Keep the vial in the original carton and protect from light.
DOSING GUIDELINES	SEE BELOW	SEE BELOW	SEE BELOW	SEE BELOW	SEE BELOW
FDA APPROVED INDICATION **FOR PATIENTS WITH HEMOPHILIA B OR FACTOR IX DEFICIENCY** **ICD-10 DIAGNOSIS CODE D67**	Prevention and control of bleeding in adults and children: ☑ Episodic bleeds ☑ Perioperative management	Prevention and control of bleeding in adults and children >12 year old: ☑ Episodic bleeds ☑ Perioperative management	Prevention and control of bleeding in adults and children: ☑ Episodic bleeds ☑ Perioperative management ☑ Routine prophylaxis -Not indicated for induction of immune tolerance in patients	Prevention and control of bleeding in adults: ☑Episodic bleeds	Prevention and control of bleeding in adults: ☑Episodic bleeds
COMMENTS	BENEFIX REQUIRES **INCREASED DOSE BY 20%** FROM STANDARD FACTOR IX DOSING FORMULA. PEDIATRIC PATIENTS REQUIRE RECOVERY STUDIES AND POTENTIALLY HIGHER DOSES.	Calculate dose using standard equation.	RIXUBIS REQUIRES **INCREASED DOSE BY 15-20%** FROM STANDARD FACTOR IX DOSING FORMULA. PEDIATRIC PATIENTS REQUIRE RECOVERY STUDIES AND POTENTIALLY HIGHER DOSES.	Calculate dose using standard equation.	Calculate dose using standard equation.

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:
FACTOR IX CONCENTRATES EXTENDED HALF-LIFE

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

	ALPROLIX™	IDELVION®	REBINYN®
MANUFACTURER	BIOVERATIV (FORMERLY BIOGEN IDEC)	CSL Behring	Novo Nordisk
US LICENSURE DATE	2014	2016	2017
CLASSIFICATION	RECOMBINANT Fc FUSION	RECOMBINANT –ALBUMIN FUSION PROTEIN	RECOMBINANT –GlycoPEGylated
CELL LINE FORMULATION, SOURCE MATERIAL	Human embryonic kidney (HEK) cell line	Chinese Hamster Ovary (CHO) cell line	Chinese Hamster Ovary (CHO) cell line
PROTEIN PURIFICATION PROCESS	Column Chromatography	N/A	Monoclonal Affinity Chromatography
VIRAL INACTIVATION METHODS	Nanofiltration	Solvent/Detergent	Solvent/Detergent Nanofiltration
STABILIZING AGENTS	Sucrose Mannitol	Albumin Sucrose	Sucrose Mannitol
INACTIVE INGREDIENTS	Sucrose, mannitol, sodium chloride, L-histidine, Polysorbate-20	Sodium citrate, polysorbate 80, mannitol and sucrose.	Sucrose, sodium chloride, histidine, mannitol, polysorbate 80,
SPECIFIC ACTIVITY (amount of clotting activity per weight of substance)	43.8 (±5.4) to 62.7 (±2.87) IU/mg	54-85 IU/mg	152 IU/mg
MEAN HALF LIFE	2-5 yrs.: 66.4 hrs. 6-11 yrs.: 72.23 hrs. 12-17 yrs.: 83.59 hrs. >17 yrs.: 86.52 hrs.	Following single 50 IU/kg dose: 0 to <6 yrs.: 90 hrs. 6 to < 12 yrs.: 93 hrs. 12 to < 18 yrs.: 87 hrs. >18 yrs.: 104 hrs.	Following single 40 IU/kg dose: ≤6 yrs.: 69.6 hrs. (±15.8 hrs.) 7-12 yrs.: 76.3 hrs. (±25.5 hrs.) 13-17 yrs.: 89.4 hrs. (±24.1 hrs.) >18 yrs.: 83 hrs. (±22.5 hrs.)
Ratio of the mean half-life of long-acting factor/rFIX	5.3	2.4	N/A
BOX CONTENTS	Diluent: 5 mL prefilled Syringe (0.325% (w/v) NaCl) with plunger stopper and tip-cap, vial adapter	Diluent: 2.5 mL (250, 500, 1000 IU), 5 mL (2000 IU) Sterile Water for Injection, one Mix2Vial filter transfer set and one sterile alcohol swab.	Diluent: 4 mL histidine diluent in MixPro® prefilled syringe and vial adapter
ASSAYS AVAILABLE	500 IU, 1000 IU, 2000 IU, 3000 IU, 4000 IU	250 IU, 500 IU, 1000 IU, 2000 IU	500 IU, 1000 IU, 2000 IU

University of Colorado Hemophilia & Thrombosis Center Pharmacy:
FACTOR IX CONCENTRATES EXTENDED HALF-LIFE

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

	ALPROLIX™	IDELVION®	REBINYN®
INFUSION RATE	≤10 mL/minute Infuse within 3 hours of reconstitution.	<10 mL/minute Infuse within 4 hours of reconstitution	10 mL/minute Infuse within 4 hours of reconstitution
STORAGE REQUIREMENTS	▫Refrigerate (36°F to 46°F) to expiration date or store at room temperature < 86 °F for up to 6 months. ▫Avoid freezing, may damage the diluent. ▫Once product has been stored at room temperature, it should not be returned to refrigerator. ▫Keep the vial in the original carton and protect from light.	▫Store in refrigerator or at room temperature (36°F to 77°F). ▫Avoid freezing, may damage the diluent. ▫Keep the vial in the original carton and protect from light.	▫Refrigerate (36°F to 46°F) to expiration date or store at room temperature < 86 °F for up to 6 months. ▫Avoid freezing, may damage the diluent.
DOSING GUIDELINES	**Routine Prophylaxis:** 50 IU/kg once weekly or 100 IU/kg every 10 days. Adjust dosing interval based on individual response. -Children under 12 years of age may have higher FIX body weight-adjusted clearance, shorter half-life, and lower recovery. Higher dose per kilogram body weight or more frequent dosing may be needed in these patients. **Minor and Moderate Bleed:** 30 to 60 IU/kg every 48 hours as needed **Major Bleed:** 80 to 100 IU/kg. May repeat dose 6-10 hours later, then every 24 hours for 3 days, then every 48 hours until healing achieved	**Routine Prophylaxis:** Patients <12 you: 40-55 IU/kg every 7 days. Adjust the dosing regimen based on individual **Patients >12 you:** 25-40 IU/kg every 7 days. If well controlled on this regime may be switched to a 14-day interval 50-75 IU/kg. **Minor and Moderate Bleed:** 30-60 IU/kg every 48-72 hours for at least 1 day or until bleeding stops and healing is achieved. **Major Bleed:** 60-100 IU/kg every 48-72 hours for 7-14 days, until bleeding stops and healing is achieved. Maintenance dose weekly.	**Minor and Moderate Bleed:** 40 IU/kg at time of bleed, if not controlled an additional dose can be given **Major Bleed:** 80 IU/kg at time of bleed, if not controlled a 40 IU/kg can be given for follow up.
FDA APPROVED INDICATION **FOR PATIENTS WITH HEMOPHILIA B OR FACTOR IX DEFICIENCY** **ICD-10 DIAGNOSIS CODE** **D67**	Prevention and control of bleeding in adults and children: ☑ On demand treatment ☑ Perioperative management ☑ Routine prophylaxis	Prevention and control of bleeding in adults and children: ☑ On demand treatment ☑ Perioperative management ☑ Routine prophylaxis	Prevention and control of bleeding in adults and children: ☑ On demand treatment ☑ Perioperative management

University of Colorado Hemophilia & Thrombosis Center Pharmacy: FACTOR IX CONCENTRATES EXTENDED HALF-LIFE

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

	ALPROLIX™	IDELVION®	REBINYN®
COMMENTS		Not indicated for ITI therapy	Not indicated for routine prophylaxis or ITI therapy **CAUTION**: The pre-filled diluent syringe is made of glass with an internal tip diameter of 0.037 inches, and is compatible with a standard Luer-lock connector. Some needleless connectors for IV catheters are incompatible with the glass diluent syringes (for example, certain connectors with an internal spike, such as Clave®/MicroClave®, InVision-Plus CS®, InVision-Plus Junior®, Bionector®), and their use can damage the connector and affect administration. To administer product through incompatible needleless connectors, withdraw reconstituted product into a standard 10 mL sterile Luer-lock plastic syringe. The one-stage clotting assay results can be significantly affected by the type of activated partial thromboplastin (aPTT) reagent used, which can result in over- or under-estimation of Factor IX activity. Avoid the use of silica-based reagents, as some may overestimate the activity of REBINYN. If a validated one-stage clotting or chromogenic assay is not available locally, then use of a reference laboratory is recommended.

Dosage and duration of treatment is dependent on the factor IX 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, careful control of replacement factor is critical.

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

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.

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

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

	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

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

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

	ALPHANATE-SD®	HUMATE-P™	WILATE®	VONVENDI™
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**

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

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

	ALPHANATE-SD®	HUMATE-P™	WILATE®	VONVENDI™
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:
SPECIALTY PRODUCTS FOR TREATMENT OF FACTOR VIII OR IX INHIBITORS & ACQUIRED HEMOPHILIA

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

	FEIBA-NF ™	NOVOSEVEN-RT®	OBIZUR™	HEMLIBRA®
MANUFACTURER	SHIRE (formerly Baxalta)	NOVO NORDISK	SHIRE (formerly Baxalta)	GENENTECH (Roche Group)
US LICENSURE DATE	1986	1999	2014	2017
CLASSIFICATION	ACTIVATED PCC (Prothrombin Concentrate Complex)	"Bypassing activity" Recombinant human coagulation Factor VIIa (rFVIIa) that promotes hemostasis by activating the extrinsic pathway of the coagulation cascade.	Recombinant analogue of porcine FVIII, the B-domain has been replaced with 24 amino acid linker.	Bispecific factor IXa- and factor X-directed antibody
FDA APPROVED INDICATION	For use in hemophilia A and B patients with inhibitors for: ☑Control and prevention of bleeding episodes ☑Perioperative management ☑Routine prophylaxis to prevent or reduce the frequency of bleeding episodes.	For use in hemophilia A or B with inhibitors, acquired hemophilia, Glanzmann's thrombasthenia with refractoriness to platelet transfusions, with or without antibodies to platelets: ☑Prevention of bleeding in surgical interventions or invasive procedures Factor VII deficiency: ☑ Prevention and control of bleeding episodes ☑ Perioperative management -Safety and efficacy of NovoSeven RT has not been established outside these approved indications.	-Treatment of bleeding episodes in adults with **acquired** Hemophilia A -Safety and efficacy of OBIZUR has not been established in patients with baseline anti-porcine factor VIII inhibitor titer greater than 20 BU.	For use in hemophilia A >12 yo with inhibitors for ☑Routine prophylaxis to prevent or reduce the frequency of bleeding episodes.
CONTENTS	FEIBA contains mainly non-activated factors II, IX, and X and mainly activated factor VII. It contains approximately equal units of factor VIII inhibitor bypassing activity and prothrombin complex factors. Anti-Inhibitor Coagulant Complex.	Activated VIIa	FVIII	Humanized monoclonal modified IgG4 antibody with a bispecific antibody structure binding factor IXa and factor X.
FACTOR II	Non-activated form			
FACTOR VII	Activated form			
FACTOR IX	Non-activated form			
FACTOR X	Non-activated form			
CELL LINE FORMULATION, SOURCE MATERIAL	Pooled human plasma	Recombinant, baby hamster kidney (BHK) cell line	Recombinant porcine, baby hamster kidney (BHK) cell line	Recombinant, Chinese Hamster Ovary (CHO)

University of Colorado Hemophilia & Thrombosis Center Pharmacy:
SPECIALTY PRODUCTS FOR TREATMENT OF FACTOR VIII OR IX INHIBITORS & ACQUIRED HEMOPHILIA

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

	FEIBA-NF ™	NOVOSEVEN-RT®	OBIZUR™	HEMLIBRA®
DOSING GUIDELINES	**Control and Prevention of bleeding**: 50-100 units/kg determined by the type of bleeding episode. **Perioperative Management**: 50-100 units/kg determined by the type of surgical intervention **Routine Prophylaxis:** 85 units/kg every other day **•Do not exceed a single dose of 100 units per kg body weight and a daily dose of 200 units per kg body due to increased risk of thromboembolic events.**	**Hemophilia A or B with inhibitor:** **Bleeding episodes:** 90 mcg/kg bolus every 2 hours, adjusted based on severity of bleeding until hemostasis is achieved. Post-hemostatic dosing every 3-6 hours for severe bleeds. **Minor surgery**: 90 mcg/kg immediately before surgery and every 2 hours during surgery and for 48 hours after surgery. Then 90 mcg/kg every 2-6 hours, until healing has occurred. **Major surgery:** 90 mcg/kg immediately before surgery and every 2 hours during surgery; then 90 mcg/kg every 2 hours for the first 5 days. Continued every 4 hours, until healing has occurred. **Congenital FVII Deficiency**: Bleeding episodes: 15-30 mcg/kg every 4-6 hours until hemostasis is achieved Surgery: 15-30 mcg/kg immediately before surgery and every 4-6 hours for the duration of surgery and until hemostasis is achieved **Acquired Hemophilia-Bleeding episode or surgery:** **Bleeding Episode:** 70-90 mcg/kg every 2-3 hours until hemostasis is achieved. Surgery: 70-90 mcg/kg immediately before surgery and every 2-3 hours for the duration of surgery and until hemostasis is achieved. **Glanzmann's Thrombasthenia**: Bleeding Episode: 90 mcg/kg every 2-6 hours until hemostasis is achieved Surgery: 90 mcg/kg immediately before surgery and repeat every 2 hours for the duration of the procedure, then 90 mcg/kg every 2-6 hours to prevent post-operative bleeding	**Bleeding Episodes:** **Minor and Moderate (superficial) muscle bleed:** **Factor VIII Level Required:** 50-100 units/dL **Initial dose:** 200 iu/kg/dose titrate subsequent doses to maintain a recommended FVIII trough levels and individual response. Dose every 4 to 12 hours, frequency may be adjusted based on clinical response and measured factor VIII levels. **Major (severe intramuscular, retroperitoneal, gastrointestinal) Bleeds:** Factor VIII Levels Required: 100-200 units/dL for acute bleed. 50-100 units/dL after acute bleed is controlled, if required. **Loading dose** : 200 iu/kg/dose, titrate subsequent doses to maintain recommended FVIII trough levels and individual clinical response. Dose every 4 to 12 hours, frequency may be adjusted based on clinical response and measured FVIII levels. •Patient's half-life may vary; titrate dose and frequency based on factor VIII recovery levels and individual clinical response. •Plasma levels of factor VIII should not exceed 200% of normal or 200 units/dL.	**Prophylaxis:** 3 mg/kg subcutaneously once weekly for first 4 weeks, then 1.5 mg/kg once weekly, 3 mg/kg once every two weeks or 6 mg/kg once every four weeks.

University of Colorado Hemophilia & Thrombosis Center Pharmacy:
SPECIALTY PRODUCTS FOR TREATMENT OF FACTOR VIII OR IX INHIBITORS & ACQUIRED HEMOPHILIA

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

	FEIBA-NF ™	NOVOSEVEN-RT®	OBIZUR™	HEMLIBRA®
PROTEIN PURIFICATION	•Ion exchange chromatography •Ultrafiltration	•Sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE)	•Chromatography • Filtration	N/A
VIRAL INACTIVATION METHODS	•Vapor Heat; nanofiltration •DEAE-Sephadex adsorption	Chromatography	•Solvent/Detergent •Nanofiltration	N/A
MEAN HALF-LIFE	FII: ~72 Hrs	Healthy Patients (ages 20-45) :3.9-6.0 hrs Hemophilia A or B (ages 15-63): 2.89 hrs FVII deficient (ages 20-43): 2.82-3.11 hrs	Variable	27.8 ±8.1 days Due to long half-life of HEMLIBRA effects on coagulation assays may persist for up to 6 months after last dose.
INACTIVE INGREDIENTS	Trisodium citrate, NaCl	Histidine, trace amounts of mouse IgG, bovine IgG, and protein from baby hamster kidney-cells	NaCl, tris-bas, tris-HCl, tri-sodium citrate dehydrate, calcium chloride dehydrate, sucrose, polysorbate-80	L-arginine, L-histadine, poloxamer 188, L-aspartic Acid
DRUG INTERACTIONS	•Consider the possibility of thrombotic events when systemic anti-fibrinolytics such as tranexamic acid and aminocaproic acid are used. •No adequate and well-controlled studies of the combined or sequential use of FEIBA and factor VIIa or anti-fibrinolytics have been conducted. Use of anti-fibrinolytics within approximately 6 to 12 hours after the administration of FEIBA is not recommended. Cases of TMA and Thrombotic events were reported from clinical trials when an average cumulative amount of > 100 IU/kg/24 hours of activated prothrombin complex concentrate (ex. Feiba) was administered for 24 hours or more to patients receiving HEMLIBRA prophylaxis.	•Avoid simultaneous use of NovoSeven and aPCCs/PCCs (activated or non-activated prothrombin complex concentrates) •Do not mix with other infusion solutions. •Do not administer NovoSeven RT with coagulation factor FXIII thrombosis may occur.		**Thrombotic Microangiopathy Associated and Thromboembolism with HEMLIBRA and APCC**. Cases of TMA and Thrombotic events were reported from clinical trials when an average cumulative amount of > 100 IU/kg/24 hours of activated prothrombin complex concentrate (ex. Feiba) was administered for 24 hours or more to patients receiving HEMLIBRA prophylaxis. There is the possibility for hypercoagulability with rFVIIa or FVIII with HEMLIBRA based on preclinical experiments.

University of Colorado Hemophilia & Thrombosis Center Pharmacy:
SPECIALTY PRODUCTS FOR TREATMENT OF FACTOR VIII OR IX INHIBITORS & ACQUIRED HEMOPHILIA

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

	FEIBA-NF ™	NOVOSEVEN-RT®	OBIZUR™	HEMLIBRA®
AVAILABLE ASSAYS	500 IU, 1000 IU, 2000 IU	1 mg (1000 mcg) , 2 mg (2000 mcg),5 mg (5000 mcg) 8 mg (8000 mcg)	500 IU	30 mg/1 mL in a single-dose vial 60 mg/0.4 mL in a single-dose vial 105 mg/0.7 mL in a single-dose vial 150 mg/1 mL in a single-dose vial
INFUSION RATE	2 units/kg/minute, A syringe pump may be used to control the rate of administration. Administer within 3 hours of reconstitution.	Slowly over 2-5 minutes After reconstitution, store either at room temperature or refrigerated for up to 3 hours. After reconstitution with specified volume of histidine diluent, the final solution contains 1mg per ml of rFVIIa.	1-2 mL/minute Use within 3 hours of reconstitution.	Subcutaneously injection
BOX CONTENTS	Diluent: 10 mL (500), 20 mL (1000), 50 mL (2500) Sterile Water for Injection, BAXJECT II high flow needleless transfer device.	One pre-filled histidine diluent syringe: 1.1 mL (1 mg) , 2.1 mL (2mg) , 5.2mL (5 mg) , 8.1 mL (8mg), vial adapter for needleless reconstitution.	Prefilled syringe with 1 mL Sterile Water for Injection, vial adapter with filter.	Vial of colorless to slightly yellow solution in single-dose vial
STORAGE REQUIREMENTS	▫Store at room temperature ≤ 25°C (77°F). ▫Do not freeze. ▫ Store in the original package and protect from light.	▫Store at room temperature 2 to 25°C (36 to 77°F). ▫Do not freeze. ▫Store in the original package and protect from light.	▫Refrigerate 2 to 8°C (36°F to 46°F) to expiration date. ▫Do not freeze. ▫Store in the original package and protect from light.	Refrigerate 2 to 8°C (36°F to 46°F) to expiration date. ▫Do not freeze. ▫Store in the original package and protect from light

University of Colorado Hemophilia & Thrombosis Center Pharmacy:
SPECIALTY PRODUCTS FOR TREATMENT OF FACTOR VIII OR IX INHIBITORS & ACQUIRED HEMOPHILIA

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

	FEIBA-NF ™	NOVOSEVEN-RT®	OBIZUR™	HEMLIBRA®
COMMENTS	**WARNING: THROMBOEMBOLIC EVENTS** Thromboembolic events have been reported during post-marketing surveillance, particularly following the administration of high doses and /or in patients with thrombotic risk factors. Monitor patients receiving FEIBA for signs and symptoms of thromboembolic events. **PRECAUTION**: FEIBA can cause thromboembolic events following doses above 200 units/kg/day and in patients with thrombotic risk. Monitor patients for signs and symptoms of thromboembolic events. Contains 1-6 units of factor VIII coagulant antigen (FVIII C:Ag) per mL.	**CAUTION**: The pre-filled diluent syringe is made of glass with an internal tip diameter of 0.037 inches, and is compatible with a standard Luer-lock connector. Some needleless connectors for IV catheters are incompatible with the glass diluent syringes (for example, certain connectors with an internal spike, such as Clave®/MicroClave®, InVision-Plus CS®, InVision-Plus Junior®, Bionector®), and their use can damage the connector and affect administration. To administer product through incompatible needleless connectors, withdraw reconstituted product into a standard 10 mL sterile Luer-lock plastic syringe. **WARNING: THROMBOSIS** • Serious arterial and venous thrombotic events following administration of NovoSeven have been reported. • Discuss the risks and explain the signs and symptoms of thrombotic and thromboembolic events to patients who will receive NovoSeven RT . • Monitor patients for signs or symptoms of activation of the coagulation system and for thrombosis. NOTE: To avoid product waste, dose should be calculated to nearest complete vial size		**WARNING AND PRECAUTIONS:** **Thrombotic Microangiopathy Associated and Thromboembolism with HEMLIBRA and aPCC**. Cases of TMA and Thrombotic events were reported from clinical trials when an average cumulative amount of > 100 IU/kg/24 hours of activated prothrombin complex concentrate (ex. Feiba) was administered for 24 hours or more to patients receiving HEMLIBRA prophylaxis. MASAC Recommendations: Use of aPCC for breakthrough bleed treatment for patients on HEMLIBRA should be avoided if possible, and rFVIIa should be the first option used to treat. If aPCC is used, it should be limited to no more than 50 IU//kg as an initial dose and not to exceed 100 IU/kg/day. **Drug-Laboratory Test Interactions**: HEMLIBRA affects intrinsic pathway clotting-based laboratory tests, including all assays based on aPTT, Bethesda assays for FVIII inhibitor titers and activated clotting time (ACT) aPTT-based assays including clot-based FVIII activity assays with yield artificially shortened aPTT Laboratory results **unaffected** by HEMLIBRA: -Chromogenic FVIII assays will only provide an assessment of HEMLIBRA activity if the assay includes all human reagents. -Thrombin time - Bethesda assays (bovine chromogenic) - One-stage, prothrombin time based, single-factor assay -Immuno-based assays (i.e. ELISA) **Due to the long half-life of HEMLIBRA, effects on coagulation assays may persist for up to 6 months after the last dose.**

NOTE: Recombinant technology may be the ONLY product of choice for patients of Jehovah's Witnesses faith.

University of Colorado Hemophilia & Thrombosis Center Pharmacy: ADDITIONAL INFUSED FACTOR PRODUCTS

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

	C-PROTEIN CONCENTRATE	FIBRINOGEN CONCENTRATE	FX	FXIII	
	CEPROTIN	RIASTAP®	COAGADEX®	CORIFACT®	TRETTEN®
MANUFACTURER	SHIRE (formerly Baxalta)	CSL BEHRING	BIO PRODUCTS LABORATORY LIMITED	CSL BEHRING	NOVO NORDISK
U.S. LICENSURE DATE	2007	2009	2015	2013	2013
CLASSIFICATION	PROTEIN C	FIBRINOGEN CONCENTRATE	PLASMA DERIVED FACTOR X	FACTOR XIII (Plasma) Pooled	FACTOR XIII (Recombinant)
SOURCE MATERIAL	Pooled Human Plasma	Pooled Human Plasma	Pooled Human Plasma	FACTOR XIII (Plasma)	Recombinant Human factor XIII-A_2 manufactured as an intracellular, soluble protein in yeast (Saccharomyces cerevisiae) production strain.
PROTEIN PURIFICATION METHOD	Immunoaffinity chromatography	Glycine precipitation	Anion exchange chromatography Salt precipitation	Ion exchange chromatography, 20nm filtration Precipitation/adsorption; Ion exchange chromatography; Heat treatment; Virus filtration	Hydrophobic interaction and ion exchange chromatography
VIRAL INACTIVATION ATTENUATION METHODPROCESS	Detergent treatment; heat inactivation; Immunoaffinity chromatography	Cryoprecipitation; absorption/precipitation; heat treatment ; glycine precipitation	Solvent/Detergent Nanofiltration Dry heat treatment	Precipitation/adsorption; Ion exchange chromatography; Heat treatment; Virus filtration	N/A
INACTIVE INGREDIENTS	Albumin, heparin, mouse protein, sodium chloride, trisodium citrate dihydrate	Albumin, l-arginine hydrochloride, NaCl, sodium citrate, NaOH, HCl	Chloride, phosphate, citrate, sucrose and sodium -Contains ≤ 1 IU/ml of FII and X in the final reconstituted product.	Human albumin, NaCl, glucose, sodium hydroxide	NaCl, sucrose, polysorbate-20, L-Histidine
MEAN HALF-LIFE	Non-compartmental approach: Mean 9.88 hours (95% CI for median 7.1-11.6; Min 4.9, Max 14.7)	78.7 ± 18.13 hours (may be shorter in pediatric patients)	30.3 hrs.	Pediatrics ≤ 16 yo: 5.7 ± 1.00 days 6.6 ± 2.29 days	5.1 days
BOX CONTENTS	Diluent: Sterile Water for Injection 5 mL (500 IU), 10 mL (1000 IU) Sterile Water, transfer needle, filter needle.	One vial of RiaSTAP. Does not include 50 mL diluent or transfer device.	Diluent: 2.5 mL (250 IU), 5ml (500 IU) Sterile Water for Injection, Mix2Vial™ transfer device.	Diluent: 20 mL Sterile Water for Injection, a Mix2Vial filter transfer set one alcohol swab.Pediatrics ≤ 16 yo: 5.7 ± 1.00 days 6.6 ± 2.29 days	Diluent: 3.2 mL Sterile Water for Injection, vial adapter
AVAILABLE ASSAYS	500 IU, 1000 IU	900 mg to 1300 mg	250 IU, 500 IU	1000-1600 IU per vial	2500 IU per vial (2000-3125 IU per vial)

University of Colorado Hemophilia & Thrombosis Center Pharmacy: ADDITIONAL INFUSED FACTOR PRODUCTS

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

	C-PROTEIN CONCENTRATE	FIBRINOGEN CONCENTRATE	FX	FXIII	
	CEPROTIN	**RIASTAP®**	**COAGADEX®**	**CORIFACT®**	**TRETTEN®**
INFUSION RATE	Not to exceed 0.2 mL/kg/minute Infuse within 3 hours of reconstitution.	Not to exceed 5 mL/minute Infuse within 8 hours of reconstitution.	10 ml/min not to exceed 20 ml/min Use within one hour of reconstitution.	Do not exceed an infusion rate greater than 4 mL/minute Use within 4 hours of reconstitution.	Do not exceed 1-2 mL/minute Use within 3 hours of reconstitution. If the reconstituted product is not used immediately, store the solution refrigerated or at room temperature not to exceed 25°C (77°F) for up to 3 hours following reconstitution.
STORAGE REQUIREMENTS	▫Refrigerate at 36°F–46°F (2°C–8°C) until expiration date. ▫Do not freeze. ▫Keep the vial in the original carton and protect from light.	▫Store room temperature ≤ 77°F (25°C) until expiration date. ▫Do not freeze. ▫Keep the vial in the original carton and protect from light.	Store in refrigerator or at room temperature < 30°C (36°F -86°F) ▫Do not freeze. ▫Store in the original package and protect from light.	▫Refrigerate 2-8 °C (36-46°F) Do not freeze and protect from light. May be stored at room temperature ≤ 25 °C (77 °F) for up to 6 months. ▫Do not freeze. ▫Do not return the product to the refrigerator after it is stored at room temperature. ▫Store vial in original box and protect from light.	▫Refrigerate 2-8 °C (36-46°F) to expiration date. ▫Do not freeze ▫Store vial in original box and protect from light and protect from light.
DOSING GUIDELINES	**Acute Episode/Short term prophylaxis:** Initial dose: 100-120 IU/kg Subsequent 3 doses: 60-80 IU/kg every 6 hours Maintenance dose: 45-60 IU/kg every 6 or 12 hours **Long-term Prophylaxis:** 45-60 IU/kg every 12 hours. NOTE: Dose, administration frequency and duration of treatment is dependent the severity of the Protein C deficiency. **The dose regimen should be adjusted according to the pharmacokinetic profile for each patient.** An initial dose of 100-120 IU/kg for determination of recovery and half-life is	RiaSTAP dose when baseline fibrinogen level is known: Dose (mg/kg body weight) = [Target level (mg/dL) - measured level (mg/dL)] 1.7 (mg/dL per mg/kg body weight) RiaSTAP dose when baseline fibrinogen level is not known: 70 mg/kg (body weight) NOTE: Monitoring of patient's fibrinogen level is recommended during treatment with RiaSTAP. A target fibgrinogen level of 100 mg/dL should be maintained until hemostasis is obtained.	**Dose (IU) =Body Weight (kg) x Desired Factor X Rise (IU/dL) x 0.5** **Bleeding episodes:** 25 IU/ kg/dose, repeated at intervals of 24 hours until the bleed stops. **For perioperative management:** **Pre-Surgery:** Increase plasma Factor X levels to 70-90 IU/dL. **Post-surgery:** Maintain plasma Factor X levels at a minimum of 50 IU/dL until the patient is no longer at risk of bleeding due to surgery. •The dosage and duration of treatment is dependent on the severity of the Factor X deficiency, on the location and extent of the bleeding and on the patient's clinical condition.	**Prophylaxis**: 40 IU/kg every 28 days **SEE PI FOR PERI-OPERATIVE AND SURICAL DOSING GUIDELINES**	**Prophylaxis:** 35 IU/kg once a month

University of Colorado Hemophilia & Thrombosis Center Pharmacy: ADDITIONAL INFUSED FACTOR PRODUCTS

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

	C-PROTEIN CONCENTRATE	FIBRINOGEN CONCENTRATE	FX	FXIII	
	CEPROTIN	**RIASTAP®**	**COAGADEX®**	**CORIFACT®**	**TRETTEN®**
DOSING GUIDELINES (Cont'd)	recommended. After resolution of acute episode, continue patient on dose to maintain a trough protein C activity level about 25%	Dose should be individually calculated for each patient based on the target plasma fibrinogen level based on the type of bleeding, actual measured plasma fibrinogen level and body weight.			
FDA APPROVED INDICATION	Pediatric and adult patients with severe congenital Protein C deficiency for the prevention and treatment of venous thrombosis and purpura fulminans.	Treatment of acute bleeding episodes in patients with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogemia. NOT indicated for dysfibrinogenemia.	For use in patients >12 years old with hereditary Factor X deficiency for: ☑Treatment and control of bleeding episodes ☑Perioperative management	Prevention and control of bleeding in adults and children: ☑Routine prophylaxis ☑Perioperative management	Prevention of bleeding in adults with factor XIII **A-subunit** deficiency: ☑**R**outine prophylaxis
COMMENTS	-Contains trace amounts of heparin that may lead to heparin-induced thrombocytopenia. -Patient on a low sodium diet should be informed that the quantity of sodium in the maximum daily dose of Ceprotin exceeds 200 mg.	Reconstitute each vial with 50 mL of Sterile Water for Injection, which is NOT included with the product.	Each vial labeled in number Factor X in international units (IU) Note: Perioperative management of bleeding in major surgery in patients with moderate and severe hereditary Factor X deficiency has not been studied.	Do not exceed an infusion rate greater than 4 mL/minute Contains factor XIII subunit A and B	No human or animal derived products used in the manufacturing process **Contains only factor XIII subunit-A** **Do not administer TRETTEN®with recombinant factor FVIIa**

NOTE: Recombinant technology may be the ONLY product of choice for patients of Jehovah's Witnesses faith.

University of Colorado Hemophilia & Thrombosis Center Pharmacy: NON-FACTOR TREATMENTS

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

	HEMLIBRA
MANUFACTURER	GENENTECH (Roche Group)
U.S. LICENSURE DATE	2017
CLASSIFICATION	Bispecific factor IXa- and factor X-directed antibody
SOURCE MATERIAL	Recombinant, Chinese Hamster Ovary (CHO)
FDA APPROVED INDICATIONS	For use in hemophilia A patients with or without inhibitors for: ☑Routine prophylaxis to prevent or reduce the frequency of bleeding episodes.
INACTIVE INGREDIENTS	L-arginine, L-histidine, poloxamer 188 and L-aspartic acid
MEAN HALF-LIFE	26.9+/- 9.1 days
DOSING GUIDELINES	Recommended Dosage : Loading dose of 3 mg/kg subcutaneous injection once weekly for the first 4 weeks followed by a maintenance dose of : • 1.5 mg/kg once every week, or • 3 mg/kg once every 2 weeks, or • 6 mg/kg once every 4 weeks
AVAILABLE STRENGTHS	30 mg/mL in a single-dose vial 60 mg/0.4 mL in a single-dose vial 105 mg/0.7 mL in a single-dose vial 150 mg/mL in a single-dose vial

University of Colorado Hemophilia & Thrombosis Center Pharmacy: NON-FACTOR TREATMENTS

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

	HEMLIBRA
DRUG ADMINISTRATION	Subcutaneous injection (limit volume to ≤ 2 mL per injection site)
DRUG INTERACTIONS	No drug-drug interaction studies have been conducted with HEMLIBRA. However, clinical experience suggests that a drug interaction exists with HEMLIBRA and aPCC. Thrombotic events reported in 0.5% of patients (2/391) and 5.4% of patients (2/37) who received at least one dose of a aPCC. Consider the benefits and risks if aPCC must be used in patient receiving HEMLIBRA prophylaxis.
MONITORING	HEMLIBRA affects intrinsic pathway clotting-based laboratory tests, including all assays based on aPTT, Bethesda assays for FVIII inhibitor titers and activated clotting time (ACT) aPTT-based assays including clot-based FVIII activity assays with yield artificially shortened aPTT **Laboratory results <u>unaffected</u> by HEMLIBRA:** • Chromogenic FVIII assays will only provide an assessment of HEMLIBRA activity if the assay includes all human reagents. • Thrombin time • Bethesda assays (bovine chromogenic) • One-stage, prothrombin time based, single-factor assay • Immuno-based assays (i.e. ELISA) **Due to the long half-life of HEMLIBRA, effects on coagulation assays may persist for up to 6 months after the last dose.**
STORAGE REQUIREMENTS	◦Refrigerate 2 to 8°C (36°F to 46°F) to expiration date. May be stored at room temperature < 30°C (86 °F) for 7 days. ▫Do not freeze. ▫Store in the original package and protect from light ◦Do not shake ◦Once removed from vial, dose should be administered immediately and any unused portion of Hemlibra should be discarded immediately.
COMMENTS	Most common adverse reactions (incidence >10%) are injection site reactions, headache, and arthralgia) Inform the patient that HEMLIBRA interferes with some laboratory tests that measure blood clotting and may cause a false reading. HEMLIBRA'S effect on coagulation assays may persist for up to 6 months after the last dose due to its long half-life.

NOTE: Recombinant technology may be the ONLY product of choice for patients of Jehovah's Witnesses faith.

University of Colorado Hemophilia & Thrombosis Center Pharmacy: PROTHROMBIN COMPLEX CONCENTRATE

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

	PROFILNINE- SD®	BEBULIN™	KCENTRA®	FEIBA-NF ™
MANUFACTURER	GRIFOLS	SHIRE (Formerly Baxtalta)	CSL BEHRING	SHIRE (formerly Baxalta)
U.S. LICENSURE DATE	2010	1970	2013	1986
CLASSIFICATION	Non-activated Factor IX Prothrombin Complex	Non-activated Factor IX Prothrombin Complex	Non-activated four-factor Prothrombin Complex Concentrate	ACTIVATED PCC (Prothrombin Concentrate Complex)
SOURCE MATERIAL	Pooled human plasma	Pooled human plasma	Pooled human plasma	Pooled human plasma
CONTENTS	FACTOR IX, VIT K dependent clotting factors	FACTOR IX, VIT K dependent clotting factors	FACTOR II, VII, IX, X, and protein C and S	Factors II, IX, and X and mainly activated factor VII. It contains approximately equal units of factor VIII inhibitor bypassing activity and prothrombin complex factors. Anti-Inhibitor Coagulant Complex.
Units of FII	≤ 225 IU/mL (No more than 150 units/100 Factor IX units)	24-38 IU/mL	380-800 units FII/500 units of Kcentra	Non-activated form
Units of FVII	≤ 52.5 IU/mL (No more than 35 units/100 Factor IX units)	10-240 IU/mL	200-500 units FII/500 units of Kcentra	Activated form
Units of FIX	100-150 IU/mL	10-60 IU/mL	400-620 units FII/500 units of Kcentra	Non-activated form
Units of FX	≤ 150 IU/mL (No more than 100 units/100 Factor IX units)	24-38 IU/mL	500-1020 units FII/500 units of Kcentra	Non-activated form
Units of Protein C			420-820 units FII/500 units of Kcentra	
Units of Protein S			240-680 units FII/500 units of Kcentra	
PROTEIN PURIFICATION METHODS	DEAE cellulose adsorption chromatography	DEAE-Sephadex® absorption chromatography	Ion exchange chromatography	Ion exchange chromatography, ultrafiltration
VIRAL INACTIVATION METHODS	Solvent/detergent, nanofiltration	Nanofiltration, vapor heated	Nanofiltration, vapor heated	Vapor Heat; nanofiltration DEAE-Sephadex adsorption
INACTIVE INGREDIENTS	NaCl, polysorbate 80, tri(n-butyl) phosphate, citric acid monohydrate, disodium phosphate dehydrate, benzalkonium chloride, purified water	Heparin, sodium citrate, NaCl	NaCl, citric acid monohydrate, disodium phosphate dehydrate, benzalkonium chloride, purified water	Trisodium citrate, NaCl
MEAN HALF LIFE	24.68 ± 8.29 hours	19.97 ± 8.24 hours	FII= 60.4 hours FVII=5 hours FIX=42.4 hours FX=31.8 hours Protein C=49.6 hours Protein S=50.4 hours	FII: ~72 Hrs
BOX CONTENTS	Diluent: 5 mL (500 IU), 10 mL (1000 IU, 1500 IU) Sterile Water for Injection, Mix2Vial transfer	Diluent: 20 mL (all sizes) Sterile Water for Injection, transfer needle, filter needle	Diluent 20 mL (500 IU), 40 mL (1000 IU) Sterile Water for Injection, Mix2Vial filter transfer set, alcohol swab	Diluent: 10 mL (500), 20 mL (1000), 50 mL (2500) Sterile Water for Injection, BAXJECT II high flow needleless transfer device
ASSAYS AVAILABLE	500 IU, 1000 IU, 1500 IU	500-700 IU	500 IU, 1000 IU	500 IU, 1000 IU, 2000 IU

University of Colorado Hemophilia & Thrombosis Center Pharmacy: PROTHROMBIN COMPLEX CONCENTRATE

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

	PROFILNINE- SD®	BEBULIN™	KCENTRA®	FEIBA-NF ™
INFUSION RATE	≤10 mL/minute Use within 3 hours of reconstitution. Do not refrigerate after reconstitution.	Not to exceed 2 mL/minute Use within 3 hours of reconstitution. Do not refrigerate after reconstitution.	Infuse at a rate of 0.12/mL/kg/min (~ 3 units/kg/min), up to a maximum rate of 8.4 mL/min (~units/min) Use within 4 hours of reconstitution.	2 units/kg/minute, A syringe pump may be used to control the rate of administration. Administer within 3 hours of reconstitution.
STORAGE REQUIREMENTS	▫Store at refrigerated temperature 2°C to 8°C (35°F to 46°) until expiration. ▫ May be stored at room temperature ≤ 30°C (86°F) for up to 3 months. ▫Do not freeze.	▫Store at refrigerated temperature 2°C to 8°C (35°F to 46°) until expiration. ▫Do not freeze.	▫Store at refrigerated temperature 2°C to 25°C (36°F to 77°F) or until expiration. ▫Do not Freeze.	▫Store at room temperature ≤ 25°C (77°F). ▫Do not freeze. ▫ Store in the original package and protect from light.
DOSING GUIDELINES	**Body wt. (kg) x 1.0 IU/kg x Desired Increase in plasma factor IX (%) = Number of Factor IX in IU required** **NOTE: The amount of Profilnine required to establish hemostasis will vary with each patient and depends on the circumstances.**	**Body wt. (kg) x desired Factor IX increase (%) x 1.2 = Number of FIX in IU required** **Minor bleed (epistaxis, mouth bleed):** 25-35 units/kg/dose X 1 day **Moderate bleed (joint bleed, minor trauma)**: 50-65 units/kg kg/dose X 2 days or until adequate wound healing **Major bleed (severe trauma, severe hematoma):** 75-90 units/kg/dose every 2-3 days or until adequate wound healing. **NOTE: The response to treatment will vary from patient to patient. Exact dosage determination should be based on localization and extent of hemorrhage and the level of Factor IX to be achieved**.	**Dosage Required for Reversal of VKA Anticoagulation in Patients with acute major bleeding or need for an urgent surgery/invasive procedure:** **If Pre-treatment INR=2-<4** give 25 units/kg, NTE 2500 units **If Pre-treatment INR=4-6** give 35 units/kg, NTE 3500 units **If Pre-treatment INR=>6** give 50 units/kg, NTE 5000 units **Individualize Kcentra dosing based on the patient's current pre-dose International Normalized Ratio (INR) value, and body weight. Administer Vitamin K concurrently to patients receiving Kcentra.** -Measurement of INR prior to treatment and close to the time of dosing is important because coagulation factors may be unstable in patients with acute major bleeding or an urgent need for surgery and other invasive procedures. -Vitamin K is administered to maintain Vitamin K-dependent clotting factor levels once the effects of Kcentra have diminished. -The safety and effectiveness of repeat dosing have not been established and it is not recommended.	**Control and Prevention of bleeding**: 50-100 units/kg determined by the type of bleeding episode. **Perioperative Management**: 50-100 units/kg determined by the type of surgical intervention **Routine Prophylaxis:** 85 units/kg every other day •**Do not exceed a single dose of 100 units per kg body weight and a daily dose of 200 units per kg body due to increased risk of thromboembolic events.**

University of Colorado Hemophilia & Thrombosis Center Pharmacy: PROTHROMBIN COMPLEX CONCENTRATE

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

	PROFILNINE- SD®	BEBULIN™	KCENTRA®	FEIBA-NF ™
FDA APPROVED INDICATIONS	For the prevention and control of bleeding in Factor IX deficient patients (hemophilia B)	For the prevention and control of bleeding in adults with Factor IX deficiency (hemophilia B)	Urgent reversal of acquired coagulation factor deficiency induced by vitamin K antagonist (warfarin) therapy in adults with acute major bleeding or need for urgent surgery/invasive procedure	For use in hemophilia A and B patients with inhibitors for: ☑Control and prevention of bleeding episodes ☑Perioperative management ☑Routine prophylaxis to prevent or reduce the frequency of bleeding episodes.
COMMENTS	▫Primary use for FIX deficient patient only. ▫Do not use in FVII deficient patients. ▫Does NOT contain heparin. ▫Monitor for thromboembolic complications during post-op period (DIC) ▫Each vial is labeled with the factor IX potency expressed in International Units (IU). Product contain natural rubber latex	▫Primary use for FIX deficient patient only. ▫Do not use in FVII deficient patients. ▫Contains ≤0.15 IU heparin per IU Factor. ▫Monitor for thromboembolic events (DVT, PE, thrombotic stroke, DIC) ▫ Bebulin is standardized in terms of Factor IX content and each vial is labeled for the Factor IX content indicated in International Units (IU).	▫Kcentra potency (units) is defined by Factor IX content . **BLACK BOX WARNING**: ARTERIAL AND VENOUS THROMBOEMBOLIC COMPLICATIONS	**WARNING: THROMBOEMBOLIC EVENTS** Thromboembolic events have been reported during post-marketing surveillance, particularly following the administration of high doses and /or in patients with thrombotic risk factors. Monitor patients receiving FEIBA for signs and symptoms of thromboembolic events. **PRECAUTION**: FEIBA can cause thromboembolic events following doses above 200 units/kg/day and in patients with thrombotic risk. Monitor patients for signs and symptoms of thromboembolic events. MASAC Recommendations: Use of aPCC for breakthrough bleed treatment for patients on HEMLIBRA should be avoided if possible, and rFVIIa should be the first option used to treat. If aPCC is used, it should be limited to no more than 50 IU//kg as an initial dose and not to exceed 100 IU/kg/day. Contains 1-6 units of factor VIII coagulant antigen (FVIII C:Ag) per mL.

NOTE: Recombinant technology may be the ONLY product of choice for patients of Jehovah's Witnesses faith.

University of Colorado Hemophilia & Thrombosis Center Pharmacy
MEDICATION CHART DISCLAIMER

Hemophilia and Thrombosis Center
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

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.