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
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	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

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	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

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	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

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	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.

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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.