AlphaNine® SD
Coagulation Factor IX (Human)

AlphaNine SD is an effective Factor IX replacement option for your patients with hemophilia B

Indication
- AlphaNine SD is indicated for the prevention and control of bleeding in patients with factor IX deficiency due to hemophilia B

Purity
- High-purity factor IX purified with dual-affinity chromatography with high specificity for coagulation factors

Efficacy
- 93% of infusions rated as excellent/good[1]
- 89% of bleedings resolved with 1 infusion[1]
- AlphaNine SD infused pre- and post-operatively has been proven to be a safe and effective treatment option for hemophilia B patients undergoing major surgery[2]

Safety
- Two specific virus-elimination steps
  - Solvent/detergent and nanofiltration

  AlphaNine SD is made from human plasma. Plasma products carry a risk of transmitting infectious agents, including viruses, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent, despite steps designed to reduce this risk.
- Prion elimination
  - Grifols has investigated the manufacturing process of AlphaNine SD for the capacity to decrease infectivity of prions, such as the Creutzfeldt-Jakob disease (CJD) or variant CJD agents. These studies provide reasonable assurance that low levels of CJD or vCJD, if present in the starting material, would be removed[3,4]

Consistent Pharmacokinetic Profile
- One IU of AlphaNine SD infused per kg of body weight raises the patient's plasma factor IX level by 1%[5]

Convenience
- Three convenient vial sizes including a 1500 IU assay range with 10mL diluent
- Single pull tab with FIX potency and lot number
- Customized plastic, needle-free, Mix2Vial® filter transfer set

AlphaNine SD has more FIX per gram of protein than reported by any other FIX product

Please see Important Safety Information on back cover and accompanying full Prescribing Information for AlphaNine SD.

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US Products	AlphaNine® SD Coagulation Factor IX (Human)	Mononine® Coagulation Factor IX (Human)	BeneFIX® Coagulation Factor IX (Recombinant)	Rixubis® Coagulation Factor IX (Recombinant)
Company	Grifols	CSL Behring	Pfizer	Baxter
Type of Concentrate	Plasma-derived	Plasma-derived	Recombinant from Chinese hamster ovary cell line	Recombinant from Chinese hamster ovary cell line
US Licensure Dates	1996	1992	1997	2013
Hemophilia B Indication	AlphaNine SD is indicated for the prevention and control of bleeding in patients with factor IX deficiency due to hemophilia B	Mononine is indicated for the prevention and control of bleeding in Factor IX, known as hemophilia B or Christmas disease	BeneFIX is indicated for: • Control and prevention of bleeding episodes in adult and pediatric patients with hemophilia B • Perioperative management in adult and pediatric patients with hemophilia B	Rixubis is indicated in adults and children with hemophilia B for: Control and prevention of bleeding episodes, perioperative management, and routine prophylaxis
Fractionation Methods for Protein Purification	Dual-affinity chromatography with polysaccharide ligand	Immunoaffinity chromatography with murine MAb ligand	Chromatography purification	Chromatography purification
Virus Inactivation and Removal Methods	Solvent detergent and nanofiltration	Immunoaffinity chromatography, chemical treatment protocol, and nanofiltration	Membrane nanofiltration	Solvent detergent and nanofiltration
Vial Sizes	500, 1000, 1500 IU	500, 1000 IU	250, 500, 1000, 2000, 3000 IU	250, 500, 1000, 2000, 3000 IU
Diluent Volume	10 mL	5 mL, 10 mL	5 mL	5 mL
Infusion Rate	≤10 mL/minute	2 mL/minute	Over several minutes according to patient's comfort level	≤10 mL/minute
Specific Activity	>225 IU FIX/mg total protein	Not less than 190 IU FIX/mg total protein	≥200 IU FIX/mg total protein	≥200 IU FIX/mg total protein
Dosing	Body weight (kg) x % increase FIX desired x 1.0 IU/kg	Body weight (kg) x % increase FIX desired x 1.0 IU/kg	*Adults ≤ 15:* Body weight (kg) x % increase FIX desired x 1.3 (IU/kg per IU/dL) *Pediatrics < 15:* Body weight (kg) x % increase FIX desired x 1.4 (IU/kg per IU/dL) Dosing of BeneFIX may differ from that of plasma-derived factor IX products. Subjects at the low end of the observed FIX recovery may require upward dosage adjustment of BeneFIX to as much as two times (2X) the initial empirically calculated dose in order to achieve the intended rise in circulating factor IX activity	Body weight (kg) x % increase FIX desired x 1.1 dL/kg *For patients < 12 years of age:* Dose (international units) = body weight (kg) x desired FIX increase (% of normal or IU/dL) x 1.4 dL/kg *For patients ≥ 12 years of age:* Dose (international units) = body weight (kg) x desired FIX increase (% of normal or IU/dL) x 1.1 dL/kg
Contraindications	None known	Known hypersensitivity to mouse protein	BeneFIX is contraindicated in patients who have manifested life-threatening, immediate hypersensitivity reactions, including anaphylaxis, to the product or its components, including hamster protein	• Known hypersensitivity to Rixubis or its excipients including hamster protein • Disseminated Intravascular Coagulation (DIC) • Signs of fibrinolysis
Storage	Stable for 3 years, up to the expiration date printed on its label, provided that the storage temperature is between 2 and 8 °C (36 and 46 °F). Do not freeze. May be stored at room temperature not to exceed 30 °C for one month.	When stored at refrigerator temperature, 2 to 8 °C (36 to 46 °F), Mononine is stable for the period indicated by the expiration date on its label. Within this period, Mononine may be stored at room temperature not to exceed 25 °C (77 °F) for up to one month.	Can be stored at room temperature or under refrigeration, at a temperature of 2 to 30 °C (36 to 86 °F), up to the expiration date on the label.	Store at refrigerated temperature; 2 to 8 °C (36 to 46 °F) for up to 24 months. Do not freeze. May store at room temperature not to exceed 30 °C (86 °F) for up to 12 months within the 24 month time period. Write on the carton the date RIXUBIS was removed from refrigeration.
Supplied Reconstitution Device	Mix2Vial® filter transfer set	Double-ended transfer needle	Vial adapter reconstitution device and prefilled diluent syringe	BAXJECT II

Alprolix® Coagulation Factor IX (Recombinant)	Ixinity® Coagulation Factor IX (Recombinant)	Idelvion® Coagulation Factor IX (Recombinant), Albumin Fusion Protein	Rebinyn® Coagulation Factor IX (Recombinant), GlycoPEGylated
Bioverativ	Aptevo BioTherapeutics	CSL Behring	Novo Nordisk
Recombinant from human embryonic kidney cell line	Recombinant from Chinese hamster ovary cell line	Recombinant from Chinese hamster ovary cell line	Recombinant from Chinese hamster ovary cell line (PEGylation)
2014	2015	2016	2017
Alprolix is indicated in adults and children with hemophilia B for: • Control and prevention of bleeding episodes • Perioperative management • Routine prophylaxis to prevent or reduce the frequency of bleeding episodes	Ixinity is indicated in adults and children ≥ 12 years of age with hemophilia B for control and prevention of bleeding episodes and for perioperative management	Idelvion is indicated in children and adults with hemophilia B (congenital factor IX deficiency) for: • On-demand treatment and control of bleeding episodes • Perioperative management of bleeding • Routine prophylaxis to reduce the frequency of bleeding episodes *Limitations of use:* Idelvion is not indicated for immune tolerance induction in patients with hemophilia B	Rebinyn is indicated for use in adults and children with hemophilia B: • On-demand treatment and control of bleeding episodes • Perioperative management of bleeding *Limitations of use:* Rebinyn is not indicated for routine prophylaxis in the treatment of patients with hemophilia B. Rebinyn is not indicated for immune tolerance induction in patients with hemophilia B.
Chromatography purification	Chromatography purification	Chromatography purification	Series of chromatographic steps, including affinity chromatography using a monoclonal antibody
Nanofiltration and column chromatography purification	Solvent detergent and nanofiltration	Solvent/detergent (polysorbate 80) and nanofiltration	Solvent detergent and nanofiltration
500, 1000, 2000, 3000 IU	250, 500, 1000, 1500, 2000, 3000 IU	250, 500, 1000, 2000, 3500 IU	500, 1000, 2000 IU
5 mL	5 mL	2.5 mL (for reconstitution of 250, 500 or 1000 IU vials) or 5 mL (for reconstitution of 2000 or 3500 IU vials)	4 mL
≤ 10 mL/minute	≤ 10 mL/minute	Do not exceed infusion rate of 10 mL per minute	Infuse the mixed solution slowly over 1 to 4 minutes as instructed by your doctor or nurse
Not reported	Unknown	Unknown	The nominal specific activity of Rebinyn is 152 IU/mg protein
Body weight (kg) x % increase FIX desired x 1.0 (IU/kg per IU/dL) Dose adjustment may be necessary in pediatric patients under 12 years of age For patients 12 years of age or older, dose adjustment is not usually required	*Initial Dose* Body weight (kg) x % increase FIX desired (% of normal or IU/dL) x reciprocal of observed recovery (IU/kg per IU/dL)	*On-Demand Treatment and Control of Bleeding Episodes and Perioperative Management* • Required Dose (IU)=Body weight (kg) x desired factor IX rise (% of normal or IU/dL x (reciprocal of recovery (IU/kg per IU/dL) • Adjust dose based on patient's clinical condition and response *Routine Prophylaxis* • Patients ≥ 12 years of age: 25-40 IU/kg body weight every 7 days. Patients who are well-controlled on this regimen may be switched to a 14-day interval at 50-75 IU/kg body weight • Patients < 12 years of age: 40-55 IU/kg body weight every 7 days	*On-Demand Treatment and Control of Bleeding Episodes:* 40 IU/kg body weight for minor and moderate bleeds, and 80 IU/kg body weight for major bleeds. Additional doses of 40 IU/kg can be given. *Perioperative Management:* Preoperative dose of 40 IU/kg body weight for minor surgery, and 80 IU/kg body weight for major surgery. As clinically needed for the perioperative management of bleeding, repeated doses of 40 IU/kg (in 1 to 3 day intervals) within the first week after major surgery may be administered. Frequency may be extended to once weekly after the first week until bleeding stops and healing is achieved.
Known history of hypersensitivity reactions, including anaphylaxis, to the product or its excipients	Known hypersensitivity to Ixinity or its excipients, including hamster protein	Idelvion is contraindicated in patients who have had a life-threatening hypersensitivity reactions to Idelvion, or its components, including hamster proteins	Rebinyn is contraindicated in patients who have known hypersensitivity to Rebinyn or its components (including hamster proteins).
Store at refrigerated temperature; 2 °C to 8 °C (36 °F to 46 °F). Do not freeze. If stored at room temperature, do not exceed 30 °C (86 °F) for a single 6 month period. On the carton, record the date when the product was removed from refrigeration.	250 IU strength only; store at 2 to 8 °C (36 to 46 °F) 500, 1000, 1500, 2000, and 3000 IU strengths: store at 2 to 25 °C (36 to 77 °F) Do not freeze. Keep the vial in the carton and protect from light. Infuse reconstituted solution immediately or within 3 hours of storage at room temperature after reconstitution. Do not refrigerate after reconstitution.	Store Idelvion in its package to protect from light Store the Idelvion package in the refrigerator or at room temperature 2 to 25 °C (36 to 77 °F). Do not freeze. Do not use Idelvion or the Sterilized Water for Injection diluent beyond the expiration date printed on the carton and vial labels.	Store Rebinyn in the original package in order to protect from light. Store Rebinyn under refrigeration at a temperature of 36 to 46 °F (2 to 8 °C) for up to 24 months from the date of manufacture until the expiration date stated on the label. Rebinyn may be stored at room temperature not to exceed 86 °F (30 °C) for up to 6 months within the 24-month time period. Record the date when the product was removed from the refrigerator in the space provided on the outer carton. The total time of storage at room temperature should not exceed 6 months. Do not return the product to the refrigerator. Do not use Rebinyn after the end of the 6-month period at room temperature storage, or after the expiration date stated on the vial, whichever occurs earlier. Do not freeze Rebinyn.
Sterile vial adapter	LUER-LOK administration syringe	Mix2Vial® filter transfer set	MixPro® pre-filled diluent syringe

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HEMOPHILIA B

FOR YOUR PATIENTS WITH HEMOPHILIA B[5]

Potency	Diluent size	NDC numbers
500 IU FIX range	10 mL	68516-3601-2 or 68516-3607-2
1000 IU FIX range	10 mL	68516-3602-2 or 68516-3608-2
1500 IU FIX range	10 mL	68516-3603-2 or 68516-3609-2

—AlphaNine SD should not be administered at a rate exceeding 10 mL/min

Important Safety Information

AlphaNine® SD (coagulation factor IX [human]) is indicated for the prevention and control of bleeding in patients with factor IX deficiency due to hemophilia B.

AlphaNine SD is made from human plasma. Plasma products carry a risk of transmitting infectious agents, including viruses, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent, despite steps designed to reduce this risk.

Incidences of thrombosis or disseminated intravascular coagulation (DIC) have been reported following administration of factor IX complex concentrates which contain high amounts of factor II, VII, and X. AlphaNine SD contains low, nontherapeutic levels of factor II, VII, and X.

Following administration in surgery patients and individuals with known liver disease, the physician should closely observe the patient for signs and symptoms of potential disseminated intravascular coagulation.

Allergic type hypersensitivity reactions, including anaphylaxis, have been reported for all factor IX products. The administration of plasma preparations may cause allergic reactions, mild chills, nausea, or stinging at the infusion site.

Nephrotic syndrome has been reported following attempted immune tolerance induction with factor IX products in hemophilia B patients with factor IX inhibitors and a history of severe allergic reactions to factor IX.

In order to minimize the possibility of thrombogenic complications, dosing guidelines should be strictly followed.

AlphaNine SD should not be administered at a rate exceeding 10 mL/ minute. Rapid administration may result in vasomotor reactions.

Please see accompanying full Prescribing Information for AlphaNine SD.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

References: 1. Lissitchkov T, et al. *Haemophilia.* 2011;17(4):590-596. **2.** Quon D, et al. *Haemophilia.* 2011;17(1):e196-e201. **3.** Belda FJ et al. 64th National Hemophilia Foundation Annual Meeting 2012. **4.** Herring S. *Haemophilia.* 2010;16 (Suppl):3-8. **5.** AlphaNine® SD (coagulation factor IX [human]) Prescribing Information. Grifols.

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