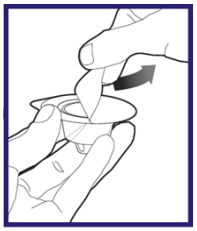
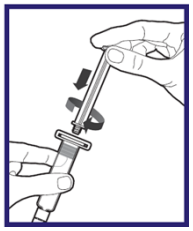
Other Names	• Antihemophilic factor IX
Description	• Produced by recombinant DNA technology in a Chinese Hamster ovary. • The cell culture medium does not contain any proteins derived from animal or human sources. • The purification process utilizes a series of chromatography steps that does not require the use of a monoclonal antibody. A membrane filtration step that has the ability to retain molecules with apparent molecular weights greater than 70,000 Da is included for additional viral safety.

Special Approvals/Authorizations	• An independent 2 person check is required for all doses. Nurses from the Manitoba Bleeding Disorder Program are exempt from the independent 2 person check.
	• A nurse may administer a dose that provides:
	  ○ Up to 200 international units greater than the prescribed dose; or
	  ○ No more than 100 international units less than the prescribed dose without receiving a new medication order.
	• Patients accustomed to self-administering Factor IX may continue to do so on the written order of a hematologist or designate.

Classification	**Special Populations:** **Pediatrics:** Safety, efficacy and pharmacokinetic studies have been evaluated in previously treated and previously untreated pediatric patients. **Geriatrics (greater than 65 years of age):** Clinical studies did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Dose selection for an elderly patient should be individualized (see Dosage and Administration). **Pregnant women:** Can be used in pregnancy only if clearly indicated. **Nursing women:** Can be used in nursing mothers if clinically indicated.

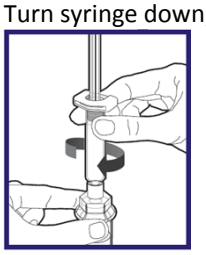
Indications	• For the control and prevention of bleeding episodes in patients with hemophilia B (congenital factor IX deficiency or Christmas disease);
	• Not indicated for the treatment of:
	  ○ Other factor deficiencies (e.g. factor II, VII, VIII, X)
	  ○ Nor for reversal of Coumarin-induced anticoagulation, nor for the treatment of bleeding due to low levels of liver-coagulation factors.

Contraindications	• Contraindicated in individuals who have manifested hypersensitivity to hamster protein and severe hypersensitivity reactions, including anaphylaxis, to the product or its components. **WARNINGS:** • The clinical response to Benefix may vary. If bleeding is not controlled with recommended dose, the plasma level of factor IX should be determined and a sufficient dose administered to achieve a satisfactory clinical response. • Allergic type hypersensitivity reactions, including anaphylaxis are possible with factor replacement therapies. • Inhibitors have been reported with factor replacement therapy. If the patient's plasma factor IX level fails to increase as expected or if bleeding is not controlled after administration, the presence of an inhibitor (neutralizing antibodies) should be suspected and appropriate testing performed. • Nephrotic syndrome has been reported following immune tolerance induction. The safety and efficacy of using Benefix for immune tolerance inductions has not been established. • Animal reproduction and lactation studies have not been conducted with Benefix.
Supplied	Vial size is 250 international units, 500 international units, 1000 international units, 2000 international

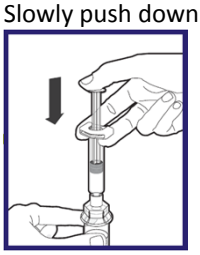
	units and 3000 international units
Dosage	**Usual:** Patient response and factor IX levels guide dose. 1 international units /kg usually raises FIX level by 1% **Treatment, Minor Hemorrhage:** 20-30 international units/kg (target FIX level 20-30%) **Treatment Moderate Hemorrhage:** 25-50 international units/kg (target FIX level 25-50 %) **Treatment, Major/Life-Threatening Hemorrhage:** 50 -100 international units/kg (target FIX level 50 -100%) **Individualized prophylaxis:** The recommended regimen is 40 international units/kg every 3-4 days.
Reconstitution/Stability	**Reconstitution:** Benefix should be reconstituted only with the diluent syringe provided in the package. Use aseptic technique throughout. 1. Allow vial of Benefix and pre filled diluent syringe to reach room temperature before use. 2. Remove the plastic flip-top cap from the Benefix vial to expose the central portions of the rubber stopper. 3. Wipe top of the vial with alcohol swab; allow to dry. 4. Peel lid back on vial adapter package. Do not remove the adapter from the package.  5. On a flat surface, place adapter over Benefix vial and push down so that the spike punctures centre of the rubber stopper on the vial.  6. Attach plunger rod to diluent syringe by inserting the rod into the syringe and turning clockwise. 

7. Hold syringe with cap pointing up; snap off cap with other hand.

8. Turn syringe down; insert tip into adapter opening on vial; turn clockwise to attach.



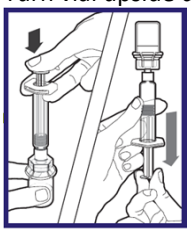
9. Slowly push down plunger of syringe to inject the diluent into the vial.



10. Swirl vial gently to dissolve the product; do not shake.

11. Do not use the reconstituted Benefix if it is cloudy or contains visible particles.

12. Turn vial upside down, slowly pull plunger rod to draw solution into syringe.



Unscrew the syringe from the vial adapter by turning the syringe counter clockwise. If you prepared more than one vial of Benefix remove the diluent syringe from the vial adapter, leaving the vial adapter attached to the vial. Attach a separate large luer lock syringe and draw back the reconstituted contents as instructed above. Repeat this procedure with each vial in turn.

	Stability: • Stable at room temperature or under refrigeration 2-30 °C until the expiry date indicated on the label. • Do not freeze. • Protect from light. • After reconstitution the product can be stored at room temperature (below 30°C) for three (3) hours. Infusions should be completed within 3 hours after reconstitution of the product. • Do NOT administer concurrently with any other product.
Compatibilities/ Incompatibilities	• No other drugs / solutions (including normal saline) can be co-administered in the same line while Benefix is being infused
Administration, Identification and ABO Compatibility	Refer to **Manitoba Best Practice Guidelines** • section 2.2 Standards - Identification and Administration • ABO Compatibility not applicable
Administration, Method	**Maximum Concentration:** • Not applicable **Maximum Rate for Initial 10 Doses:** • 0.5 – 1 mL/minute times 2 minutes. If they tolerate it, increase the rate to 1-2 mL/minute until completion of dose. If patient complains of bad taste, headache, flushing, nausea, or states that they feel unwell, drop rate back to 0.5 mL/minute. **Maximum Rate for Subsequent Doses:** • 1 – 2 mL/minutes **IV Push:** • For dose 1-10 see REQUIRED MONITORING. • For dose 11 and beyond: 1-2 mL/minute through port closes to vein. Adjust rate to patient. Flush 3-5 mL normal saline. No flush required if winged infusion set used. • The rate of administration should be determined by the patient's comfort level, and no faster than 10 mL per minute. **IV Continuous:** • The administration of Benefix by continuous infusion has not been sufficiently evaluated. Administer per protocol specified by Hematologist ONLY. **REQUIRED MONITORING:** If lifetime exposure less than 10 factor IX treatments (e.g., Benefix and/or Immunine, Alprolix), obtain baseline vital signs, then monitor for vasomotor, hypersensitivity and cardiovascular reactions for at least 60 minutes from the start of infusion. If patient receiving the first to tenth dose of treatment, start administration at 0.5 mL/minute times 2 minutes. If they tolerate it, increase the rate to 1 mL/minute until completion of dose. If patient complains of bad taste, headache, flushing, nausea, or states that they feel unwell, drop rate back to 0.5 mL/minute. Stop infusion and contact physician if hypersensitivity, vasomotor or cardiovascular reactions occur.
Adverse Events	**ADVERSE REACTIONS REPORTED:** GENERAL DISORDERS Infusion site pain, infusion site reaction, pyrexia, chest discomfort INFECTIONS AND INFESTATIONS Infusion-site cellulitis IMMUNE SYSTEM DISORDERS Hypersensitivity NERVOUS SYSTEM DISORDERS Headache, dizziness, dysgeusia, somnolence, tremors EYE DISORDERS Visual impairment GASTROINTESTINAL DISORDERS Nausea, vomiting, diarrhea VASCULAR DISORDERS

	Hypotension, phlebitis, flushing CARDIAC DISORDERS Tachycardia VASCULAR Hypotension, phlebitis RESPIRATORY Cough,respiratory distress GASTROINTESTINAL DISORDERS Vomitting, nausea SKIN AND SUBCUTANEOUS Rash, urticaria, hives RENAL and URINARY Renal infarct SYSTEMIC Chills
References:	Benefix Product Monograph – Date of Approval: April 14, 2016 Package Insert - Benefix
Reviewed By:	Dr. Donald Houston Dr. Jayson Stoffman