Other Names	• Antihemophilic factor VIII
Description	• Produced by genetically engineered baby hamster kidney cells into which the human factor VIII gene has been introduced. • Kovaltry has the identical FVIII amino acid sequence, the same molecular formula, proteolytic process and similar post translation modifications (glycosylation and sulfation) as the licensed Kogenate FS. • Oligosaccharide characterization of the final product has shown superior glycosylation, better branching, and sialylation capping of terminal galactose residues. • Human and animal derived raw materials are not used in the cell culture, purification and formulation processes. • To achieve a high virological safety level the manufacturing process incorporates dedicated viral clearance steps which include a detergent virus inactivation step and a 20 nm filtration step • The purification process includes methods of ion exchange chromatography, monoclonal antibody immunoaffinity chromatography, and other chromatographic steps designed to purify recombinant Factor VIII and remove process and product related impurities.

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 VIII may continue to do so on the written order of a hematologist or designate.

Classification	**Special Populations:** **Pediatrics (less than 12 years of age):** Kovaltry is appropriate for use in pediatric patients. **Geriatrics (greater than 65 years of age):** Clinical studies did not include subjects aged 65 and over. As with any patient receiving rFVIII, dose selection for an elderly patient should be individualized. **Pregnant women:** Animal reproduction studies have not been conducted. Factor VIII should be used during pregnancy only if clearly indicated. **Nursing women:** Experience regarding the use of factor VIII during breast-feeding is not available. Should only be administered to nursing mothers if clearly indicated.

Indications	• For the control and prevention of bleeding episodes in patients with hemophilia A
	• Peri-operative management (surgical prophylaxis)
	• Immune tolerance
	• Not indicated for the treatment of:
	  ○ Other factor deficiencies (e.g. factor II, VII, X) or for hemophilia A patients with inhibitors to factor FVIII.
	  ○ Patients with von Willebrand disease.

Contraindications	• Contraindicated in individuals who have manifested severe hypersensitivity reactions, including anaphylaxis, to the product or its components. **WARNINGS:** • The clinical response to Kovaltry, may vary. If bleeding is not controlled with recommended dose, the plasma level of factor VIII should be determined and a sufficient dose of Kovaltry 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 VIII 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. • Dose adjustment for patients with renal or hepatic impairment has not been studies in clinical trials. • Kovaltry has been shown to be non-mutagenic and non-cacogenic in mammalian cells in the mouse lymphoma assay.
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 VIII levels guide dose. 1 international units/kg usually raises FVIII level by 2% **Treatment, Minor Hemorrhage:** 10-20 international units/kg (target FVIII level 20-40%) **Treatment, Moderate to Major/Hemorrhage:** 15-30 international units/kg (target FVIII level 30-60%) **Treatment Life-Threatening Hemorrhage**: 30-50 international units/kg (target FVIII level 60-100%) **Minor Surgery:** 15-30 international units/kg (target FVIII 30-60%) **Major Surgery:** 40-50 international units/kg (target FVIII pre and post operative 80-100% **Individualized prophylaxis:** **Adults and adolescents (greater than 12 years of age):** The recommended regimen is 20 - 40 international units/kg three times per week. **Children (less than or equal to 12 years of age):** The recommended dose is 20 – 50 international units/kg twice weekly, three times weekly or EOD.
Reconstitution/Stability	**Reconstitution:** Kovaltry should be reconstituted only with the diluent syringe provided in the Kovaltry package. Use aseptic technique throughout. 1. Allow vial of Kovaltry and pre filled diluent syringe to reach room temperature before use. 2. Remove protective cap from the vial and aseptically cleanse the rubber stopper with alcohol being careful not to handle the rubber stopper. 3. Place product vial on a firm, non-skid surface. Peel off the plastic cover on the vial adapter plastic housing. Do not remove the adapter from the plastic housing. Holding the adapter housing, place over the product vial and firmly press down. The adapter will snap over the vial cap. Do not remove the adapter housing at this step. 4. Holding the syringe by the barrel, snap the syringe cap off the tip. **Do not touch the syringe tip with your hand or any surfaces.** Set the syringe aside for further use. 5. Now remove and discard the adapter plastic housing. 6. Attach the prefilled syringe to the vial adapter thread by turning clockwise. 7. Remove the clear plastic plunger rod from the carton. Grasp the plunger rod by the top plate**. Avoid touching the sides and threads of the plunger rod.** Attach the plunger rod by turning it clockwise into the threaded rubber stopper of the prefilled syringe. 8. Inject the diluent **slowly** by pushing down on the plunger rod. 9. Swirl vial gently until all powder on all sides of the vial is dissolved**. Do not shake vial.** Be sure that all powder is completely dissolved. **Do not use if solution contains visible particles or is cloudy.** 10. Push down on the plunger to push all air back into the vial. Then while holding the plunger down, turn the vial with syringe upside-down (invert) so the vial is now above the syringe. 11. Withdraw all the solution into the syringe by pulling the plunger rod back slowly and smoothly. Tilt the vial to the side and back to make sure all the solution has been drawn toward the large opening in the rubber stopper and into the syringe**. Remove as much**

	air as possible before removing the syringe from the vial by slowly and carefully pushing the air back into the vial. 12. Detach the syringe with plunger rod from the vial adapter by turning counter-clockwise. 13. Attach the syringe to the administration set provided (or provider preference set) and inject intravenously. **Stability:** • Stable at 2-8 ºC until the expiry date indicated on the label. • May be stored at room temperature up to 25 ºC for 12 months. • Once product is removed from the refrigerator, it cannot be returned to the refrigerator. • Do not freeze. • Protect from exposure light and store the lyophilized powder in the carton prior to use. • The reconstituted must be used within 3 hours. • Compatible to flush IV line with normal saline • Do NOT administer reconstituted Kovaltry in same tubing or container with other medications.
Compatibilities/ Incompatibilities	• No other drugs / solutions (including normal saline) can be co-administered in the same line while Kovaltry 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: • Kovaltry should be injected over several minutes with the rate of administration determined by the patient's response. Determine the pulse rate before and during administration. If there is a significant increase in pulse rate, reduce the rate of administration or temporarily half the infusion allowing the symptoms to disappear.
Adverse Events	• The most common adverse drug reactions were related to potential hypersensitivity reactions, including headache, pyrexia, pruritus, rash, and abdominal discomfort. • One subject was withdrawn from study due to an adverse drug reaction of rash. • There were no reports of any anaphylactic reactions or inhibitor formation in the clinical trials. **ADVERSE REACTIONS REPORTED:** GENERAL DISORDERS Chest discomfort, injection site reactions, pyrexia NERVOUS SYSTEM DISORDERS Dizziness, dysgeusia, headache GASTROINTESTINAL DISORDERS Abdominal pain, abdominal discomfort, dyspepsia VASCULAR DISORDERS Flushing CARDIAC DISORDERS Palpitation, sinus tachycardia BLOOD AND LYMPHATIC SYSTEM DISORDERS Lymphadenopathy IMMUNE SYSTEM DISORDERS Hypersensitivity PSYCHIATRIC DISORDERS Insomnia SKIN DISORDERS Dermatitis allergic, pruritus, rash, urticaria
References:	Kovaltry Product Monograph – Date of Approval: January 27, 2016 Patient Medication Information
Reviewed By:	Dr. Donald Houston Dr. Jayson Stoffman