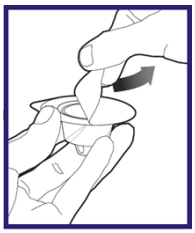
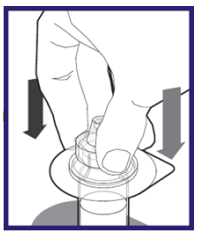
Other Names	• Antihemophilic factor VIII
Description	• Nuwiq is a fourth-generation recombinant FVIII concentrate. • Produced by DNA technology in genetically modified human embryonic kidney 293F cells with no animal or human derived materials added during the manufacturing process or to the final medicinal product. • Nuwiq contains post-translational modifications comparable to human plasma-derived FVIII and is devoid of antigenic Neu5Gc or α-1, 3-Galepitop. • Nuwiq is produced in a human cell line that has been demonstrated to be free of any endogenous or infectious viruses. The purification process includes chemical S/D treatment with a solvent, tri-(n-butyl) phosphate (TNBP) and a detergent, Triton X-100 (OcToxynol) is included for inactivation of enveloped viruses and nanofiltration is included for removal of non-enveloped viruses. Further clearance of potentially present viruses can be expected from the purification process itself, however the clearance capacity of these steps has not been formally evaluated.

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.

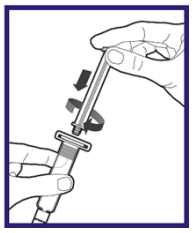
Classification	**Special Populations:** **Pediatrics (less than 12 years of age):** Nuwiq is appropriate for use in previously treated (greater than or equal to 50 exposure days) pediatric patients. Studies in previously untreated patients are ongoing. **Geriatrics (greater than 65 years of age):** No information available. **Pregnant and nursing women:** Animal reproduction studies have not been conducted. Factor FVIII should be used during pregnancy only if clearly indicated.

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

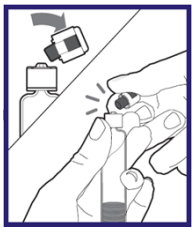
Contraindications	• Contraindicated in individuals who have manifested severe hypersensitivity reactions, including anaphylaxis, to the product or its components. **WARNINGS:** • The clinical response to Nuwiq, may vary. If bleeding is not controlled with recommended dose, the plasma level of factor VIII should be determined and a sufficient dose of Nuwiq 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
Supplied	Vial size is 250 international units, 500 international units, 1000 international units, 2000 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 two or three times per week. **Children (less than or equal 12 years of age):** The recommended dose is 20 – 50 international units/kg EOD or three times weekly.
Reconstitution/Stability	**Reconstitution:** Nuwiq should be reconstituted only with the diluent syringe provided in the Nuwiq package. Use aseptic technique throughout. 1. Allow vial of Nuwiq and pre filled diluent syringe to reach room temperature before use. 2. Remove the plastic flip-top cap from the concentrate vial to expose the central portion of the rubber stopper Do not remove the gray stopper or metal ring around the top of the vial Wipe the top of the vial with an alcohol swab (not provided). Allow the alcohol to dry. 3. Peel back the paper cover from the vial adapter package. Do not remove the adapter from the package.  4. Place the concentrate vial on an even surface and hold it. Take the adapter package and place the vial adapter over the centre of the rubber stopper of the concentrate vial. Press down firmly the adapter package until the adapter spike penetrates the rubber stopper. The adapter snaps to the vial when done. 

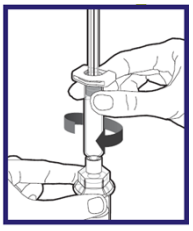
5. Peel back the paper cover from the prefilled syringe package. Take the plunger rod at the end and avoid contact with the shaft. Attach the threaded end of the plunger rod to the solvent syringe plunger. Turn the plunger rod clockwise until a slight resistance is felt.



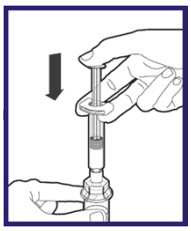
6. Break off the tamper-proof plastic tip from the solvent syringe by snapping the perforation of the cap. Do not touch the inside of the cap or the syringe tip.

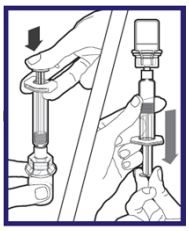
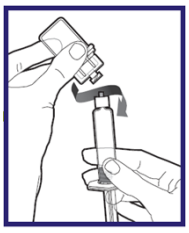


7. Remove the adapter package and discard.
8. Firmly connect the solvent syringe to the vial adapter by turning clockwise until resistance is felt.



9. Slowly inject all solvent into the concentrate vial by pressing down the plunger rod.



	10. Without removing the syringe, dissolve the concentrate powder by gently moving or swirling the vial in circles a few times. DO NOT SHAKE. Wait until all the powder dissolves completely.  11. Inspect the final solution for particles before administration. The solution should be clear and colourless, practically free from visible particles. Do not use solutions that are cloudy or have deposits. 12. Turn the vial attached to the syringe upside down, and slowly draw the final solution into the syringe. Make sure the entire content of the vials is transferred to the syringe.  13. Detach the filled syringe from the vial adapter by turning counter clockwise and discard the empty vial.  **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 up to one month not to exceed the expiration date. • Once product is removed from the refrigerator, it cannot be returned to the refrigerator. • Do not freeze. • Keep the vial in the outer carton in order to protect from light. • The reconstituted solution should be kept at room temperature (up to 25 ºC) and must be used within 3 hours. • Compatible to flush IV line with normal saline. • Do NOT mix Nuwiq with other medicinal products.
Compatibilities/ Incompatibilities	• No other drugs / solutions (including normal saline) can be co-administered in the same line while Nuwiq 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: • Administer at a rate of 4 mL per minute.
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 Injection site inflammation, injection site pain NERVOUS SYSTEM DISORDERS Paresthesia and headache GASTROINTESTINAL DISORDERS Dry mouth Muscolosketal and connective tissue disorders MUSCULOSKELETS AND CONNECTIVE TISSUE DISORDERS Backpain IMMUNE SYSTEM DISORDERS Hypersensitivity or allergic reactions (which may include angioedema, burning and stinging at the infusion site, chills, flushing, generalized urticaria, headache, hives, hypotension, lethargy, nausea, restless, tachycardia, tightness of the chest, tingling, vomiting, or wheezing) have rarely been observed with FVIII preparation and may in some cases progress to severe anaphylaxis (including shock). EAR AND LABYRINTH DISORDERS
References:	Nuwiq Product Monograph – Date of Approval: August 6, 2015 Patient Medication Information
Reviewed By:	Dr. Donald Houston Dr. Jayson Stoffman