Other Names	• Antihemophilic factor VIII
Description	• Xyntha is a recombinant human factor VIII molecule produced by genetically engineered Chinese hamster ovaries into which the human factor VIII gene has been introduced. • Prepared by a modified process that eliminates exogenous human and animal derived protein in the cell culture, purification and formulation processes. • To achieve a high virological safety level the manufacturing process incorporates a solvent-detergent virus inactivation step and a 20 nm filtration.

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):** Xyntha is appropriate for use in children of all ages, including newborns. **Geriatrics (greater than 65 years of age):** Clinical studies did not include sufficient subjects aged 65 and over. As with any patient receiving recombinant FVIII (rFVIII), dose selection for an elderly patient should be individualized.

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

Contraindications	• Contraindicated in individuals who have manifested hypersensitivity reactions to any of the constituents of the preparation or known hypersensitivity to hamster proteins. **WARNINGS:** • The clinical response to Xyntha may vary. If bleeding is not controlled with recommended dose, the plasma level of factor VIII should be determined and a sufficient dose of Xyntha 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 is not recommended, though this has not been specifically studied in clinical trials. • Xyntha has been shown to be non-mutagenic and non-carcinogenic in mouse micronucleus 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. Individual-patient pharmacokinetic studies are recommended. If such information is not available, the following guide may be used: 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 to 12 years of age):** The recommended dose is 20 – 50 international units/kg twice weekly, three times weekly or EOD.
Reconstitution/Stability	**Xyntha Vial Kit – R2:** Use only the materials provided in the Xyntha kit for dissolving the Xyntha powder with the sodium chloride diluent. Use aseptic technique throughout.   1. Allow vial of Xyntha powder and pre filled diluent syringe to reach room temperature before use. 2. Remove plastic flip-top cap from the Xyntha vial to expose the central portions of the rubber stopper.  3. Wipe the top of the vial with the alcohol swab provided, or use another antiseptic solution, and allow to dry. After cleaning, do not touch the rubber stopper with your hand or allow it to touch any surface.  4. Peel back the cover from the clear plastic vial adapter package. Do not remove the adapter from the package. 

5. Place the vial on a flat surface. While holding the adapter in the package, place the vial adapter over the vial. Press down firmly on the package until the adapter snaps into place on top of the vial, with the adapter spike penetrating the vial stopper.

6. Grasp the plunger rod as shown in the diagram. Avoid contact with the shaft of the plunger rod. Attach the threaded end of the plunger rod to the diluent syringe by pushing and turning firmly.

7. Break off the tamper-resistant, plastic-tip cap from the diluent syringe by snapping the perforation of the cap. This is done by bending the cap up and down until the perforation is broken. Do not touch the inside of the cap or the syringe tip. The diluent syringe may need to be recapped (if the dissolved Xyntha is not used immediately), so place the cap on its top on a clean surface in a spot where it would be least likely to become contaminated.

8. Lift the package away from the adapter and discard the package.

9. Place the vial on a flat surface. Connect the diluent syringe to the vial adapter by inserting the tip of the syringe into the adapter opening while firmly pushing and turning the syringe clockwise until the connection is secured.

10. Slowly depress the plunger rod to inject all the diluent into the Xyntha vial.

11. With the syringe still connected to the adapter, gently swirl the contents of the vial until the powder is dissolve.

12. Inspect the final solution for particulate matter before administration. The solution should be clear to slightly pearly and colorless. It is not, the solution should be discarded and a new kit should be used.

13. Ensuring that the syringe plunger rod is still fully depressed, invert the vial. Slowly draw the solution into the syringe.

14. If you prepared more than one vial of Xyntha, remove the diluent syringe from the vial adapter, leaving the vial adapter attached to the vial. Quickly attach a separate large luer lock syringe and draw back the dissolved contents as instructed above. Repeat this procedure with each vial in turn. Do not detach the diluent syringes or the large luer lock syringe until you are ready to attach the large luer lock syringe to the next vial adapter.

15. Detach the syringe from the vial adapter by gently pulling and turning the syringe couterclockwise. Discard the vial with the adapter attached.

Xyntha Solufuse:

1. Allow the prefilled dual-chamber syringe of freeze-dried Xyntha to reach room temperature.

2. Remove the contents of the Xyntha Solufuse Kit and place on a clean surface, making sure you have all the supplies you will need.

3. Grasp the plunger rod and avoid contact with the shaft of the plunger rod. Screw the plunger rod firmly into the opening in the finger rest of the Xyntha Solufuse by pushing and turning firmly until resistance is felt.

4. Once the white tamper-evident seal is removed it is important to keep the Xyntha Solofuse in the upright position throughout the reconstitution process to prevent possible leakage.

5. Holding the Xyntha Solofuse upright, remove the white tamper-evident seal by bending the seal right to left (or a gentle rocking motion) to break the perforation of the cap and expose the grey rubber tip cap of the Xyntha Solofuse.

6. Remove the protective blue vented sterile cap from its package. While holding the Xyntha Solofuse upright, remove the grey rubber tip cap and replace it with the protective blue vented cap (prevents pressure build-up). Avoid touching the open end of both the syringe and the protective blue vented cap.

7. Gently and slowly advance the plunger rod by pushing until the two stoppers inside the Xyntha Solofuse meet, and all of the diluent is transferred to the chamber containing the Xyntha power.


8. With the Xyntha Solofuse remaining upright, swirl gently several times until the powder is dissolved.

9. The final solution should be inspected visually for particulate matter before administration. The solution should be clear to slightly pearly and colorless. If it is not, the solution should be discarded and a new kit should be used.

10. Again, holding the Xyntha Solufuse in an upright position, slowly advance the plunger rod until most, but not all of the air is removed from the drug product chamber.






Combining Multiple Solofuse Syringes:

1. 

2. 


3. 


4. 

5. 

Combined Use of a Xyntha Vial Kit – R2 and a Xyntha Solofuse Kit

1. Reconstitute the Xyntha vial using the instructions previously provided.


2. Detach the empty diluent syringe from the vial adapter by gently turning and pulling the syringe counterclockwise, leaving the contents in the vial and the vial adapter in place.

3. Reconstitute the Xyntha Solufuse using the instructions previously provided remembering to remove most, but not all, of the air from the drug product chamber.

4. After removing the protective blue vented cap, connect the Xyntha Solofuse to the vial adapter by inserting the tip into the adapter opening while firmly pushing and turning the syringe clockwise until secured.


5. Slowly depress the plunger rod of the Xyntha Solofuse until the contents empty into the Xyntha vial. The plunger may move back slightly after release.

6. Detach and discard the empty Xyntha Solufuse from the vial adapter.

7. Connect a sterile 10 cc or larger luer lock syringe to the vial adapter. You may want to inject some air into the vial to make withdrawing the vial contents easier.

	8. Invert the vial and slowly draw the solution into the 10 cc or larger luer lock syringe.  9. Detach the syringe from the vial adapter by gently turning and pulling the syringe counterclockwise. Discard the vial with the adapter attached. **Multiple Xyntha Solofuse Reconstitution to a 10 cc or larger luer lock syringe:** 1. Reconstitute all Xyntha Solofuse according to instructions previously provided. 2. Holding the Xyntha Solofuse in an upright position, slowly advance the plunger rod until most, but not all, of the air is removed from the drug product chamber. 3. Remove the luer to luer syringe connector from its package. 4. After removing the protective blue vented cap, connect a sterile 10 cc or larger luer lock syringe to one opening (port) in the syringe connector and the Xyntha Solofuse to the remaining open port on the opposite end. 5. With the Xyntha Solofuse on top, slowly depress the plunger rod until the contents empty into the 10 cc or larger luer lock syringe. 6. Remove the empty Xyntha Solofuse and repeat procedures 3 and 4 above for any additional reconstituted syringes. 7. Remove the luer to luer syringe connector from the 10 cc or larger luer lock syringe and attach the infusion set. • Stable at 2-8 ºC until the expiry date indicated on the label. • May be stored at room temperature up to 25 ºC for 3 months. • After room temperature storage, the product can be returned to refrigerated storage until the expiration date. Do not store Xyntha at room temperature and return it to refrigerated storage more than once. • Do not freeze. • Protect from prolonged exposure to light. • The reconstituted solution must be used within 3 hours. • Compatible to flush IV line with normal saline • Do NOT administer reconstituted Xyntha 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.
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: • Xyntha should be injected over several minutes with the rate of administration determined by the patient's response.
Adverse Events	• The most common adverse reaction, on a per infusion basis was vomiting. • Drug reactions related to potential hypersensitivity reactions are possible. Manifestations may include hives, generalized urticaria, tightness in chest, wheezing, hypotension and anyaphylaxis. including headache, pyrexia, pruritus, rash, and abdominal discomfort.

	ADVERSE REACTIONS REPORTED: IMMUNE DISORDERS Anaphylactoid reaction NERVOUS SYSTEM DISORDERS Dizziness, neuropathy, increased perspiration, somnolence, altered tase GASTROINTESTINAL DISORDERS Anorexia, diarrhea, abdominal pain MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS Arthalgia, myaligia CARDIAC DISORDERS Angina pectoris, tachycardia, palpitations RESPIRATORY DISORDERS Increased cough, dyspnea VASCULAR DISORDERS Bleeding/hematoma, flushing, thrombophlebitis, hypotension, vasodialtion SKIN AND SUBCUTAENOUS TISSUE DISORDERS Pruritis, rash, urticaria GENERALD DISORDERS & ADMINISTRATION CONDITIONS Fever, Asthenia, Chills, injection site pain, injection site reaction, injection site inflammation, permanent venous access catheter complications
References:	Xyntha Product Monograph – Date of Approval: January 12, 2015 Patient Medication Information
Reviewed By:	Dr. Donald Houston Dr. Jayson Stoffman