Other Names

- Eptacog alfa (activated)
- Activated recombinant FVIIa

Description

- Niastase RT® is secreted from BHK (baby hamster kidney) cells and converted to the active form (recombinant factor VIIa) during the purification process.
- Niastase RT® (eptacog alfa, activated) is structurally similar to human plasma-derived Factor VIIa.
- Vitamin K-dependent glycoprotein consisting of 406 amino acids.

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 units greater than the prescribed dose; or
  - No more than 100 units less than the prescribed dose without receiving a new medication order.
- Patients accustomed to self-administering Niastase® may continue to do so on the written order of a hematologist or designate.

Classification

Special Populations:

- Pediatrics (birth to 16 years of age):
  Evidence for the safety and effectiveness of rFVIIa has been obtained in the age groups up to 16 years of age.
- Pregnancy and nursing:
  Data on a limited number of exposed pregnancies indicate no adverse effect on pregnancy or health of the fetus/new-born child. However use of Niastase RT® should be avoided during pregnancy. Thrombotic events such as myocardial infarction, pulmonary embolism, deep venous thrombosis, retinal artery occlusion or cerebral ischemia have been observed in patients receiving rFVIIa during delivery or post-partum.
  Unknown whether rFVIIa is excreted in human breast milk.
- Geriatrics (greater than 65 years of age):
  Clinical studies did not include sufficient numbers of subjects to determine whether they respond differently from younger subjects.

Indications

- Hemophilia A/B patients with inhibitors to FVIII and FIX, for the treatment of bleeding episodes (including treatment and prevention of those occurring during and after surgery).
- Treatment of severe bleeding episodes in Glanzmann’s thrombasthenia with clinical refractoriness and/or platelet-specific antibodies, or where platelets are not immediately available.
- Prevention of bleeding in surgical interventions or invasive procedures in Glanzmann’s thrombasthenia with clinical refractoriness and/or platelet-specific antibodies, or where platelets are not readily available.
- Adult patients with acquired hemophilia, for the treatment of bleeding episodes, and for the prevention of bleeding in those undergoing surgery or invasive procedures.

Contraindications

- Patients with rare hereditary problems of fructose intolerance, glucose malabsorption or sucrroseisomaltase insufficiency should not take this medicine.
- Simultaneous use of prothrombin complex concentrates, activated or not, should be avoided.

WARNINGS:

- Both arterial and venous thromboembolic adverse events have been reported after treatment with rFVIIa, mostly in patients with predisposing concurrent risk factors. Risk is considered low.
- Reports of fatal and non-fatal outcomes, including those associated with thromboembolic events
have been received during off-label use of Niastase RT®.

- Patients with disseminated intravascular coagulation (DIC), advanced atherosclerotic disease, crush injury, septicaemia, concomitant treatment with aPCCs/PCCs (activated or non-activated prothrombin complex concentrates) may have an increased risk of developing thrombotic events due to their underlying condition or concomitant treatment.
- Because of the risk of thromboembolic complications caution should be exercised when administering Niastase RT® to patients with a history of coronary heart disease, to patients with liver disease, to patients immobilized post-operatively, to neonates, or to patients at risk of thromboembolic phenomena or DIC. In each of these situations potential benefit should be weighed against the risk of these complications.
- Patients with inherent factor VII deficiency may have pre-existing or may develop anti-Factor VII antibodies during therapy. The clinical significance of these antibodies is unknown.

<table>
<thead>
<tr>
<th>Supplied</th>
<th>Vial size is 1.0 mg, 2.0 mg, 5.0 mg</th>
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<tr>
<th>Dosage</th>
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**Recommended dose in hereditary severe FVII deficient patients:**

Bleeding episodes: 15-30 mcg/kg at 4 to 6 hours intervals.

**Recommended dose in congenital hemophilia A or B with inhibitors:**

Bleeding episodes: 90 mcg/kg every 2 hours until clinical improvement is observed and increased to 6 hours depending on the period of time the treatment is judged to be indicated.

Surgery: Initial dose of 90 mcg/kg given immediately before the intervention and repeated every 2 hours during the procedure and increased to 6 hours depending on the clinical status of the patient and surgery.

**Recommended dose in Glanzmann’s thrombasthenia:**

Bleeding episodes: 90 mcg/kg repeated every 2-6 hours until hemostasis is achieved.

Surgery: Initial dose of 90 mcg/kg given immediately before the intervention and repeated at 2 hour intervals for duration of surgery. Post-surgical doses should be administered at 2-6 hour intervals to prevent post-operative bleeding.

**Recommended dose in acquired hemophilia:**

Bleeding episodes and surgery: 90 mcg/kg as initial dose. Initial interval should be 2-3 hours. Once hemostasis achieved the dose interval can be increased to every 4, 6, 8, or 12 hours for as long as judged to be indicated.

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<tr>
<th>Reconstitution and Stability</th>
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**Reconstitution:**

Niastase RT® should be reconstituted only with the diluent syringe provided in the package. Use aseptic technique throughout.

1. Allow vial of Niastase RT® and pre filled diluent syringe to reach room temperature before use. You can do this by holding them in your hands until they feel as warm as your hands.

2. Remove the plastic flip cap from the 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.

3. Wipe the top of the vial with an alcohol swab (not provided). Allow the alcohol to dry.

4. Peel back the paper cover from the vial adapter package. Do not remove the adapter from the package.
5. 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.

6. 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.

7. 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.

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

10. Slowly inject all solvent into the concentrate vial by pressing down the plunger rod.
11. 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.

12. 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.

13. 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.

14. Detach the filled syringe from the vial adapter by turning counter clockwise and discard the empty vial.

**Stability:**
- Store refrigerated or between 2-25°C until the expiry date indicated on the label.
- After reconstitution Niastase RT® may be stored either at room temperature (below 25°C) or refrigerated for up to 3 hours.
- Do not freeze.
- Compatible to flush IV line with normal saline.

**Compatibilities/Incompatibilities**
- Niastase RT® should not be mixed any other medications or intravenous infusion solutions or be given in a drip.

*Administration,* Refer to **Manitoba Best Practice Guidelines**
## Identification and ABO Compatibility
- section 2.2 Standards- Identification and Administration
- ABO Compatibility not applicable

## Administration, Method

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<tr>
<th>Maximum Concentration:</th>
<th>Not applicable</th>
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<tr>
<td>Maximum Rate:</td>
<td>Inject Niastase RT® slowly over 2 to 5 minutes.</td>
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## Adverse Events
- The most common adverse drug reactions were thrombotic events.
- The most common adverse reaction in patients with congenital hemophilia A or B with inhibitors were pyrexia, injection site reaction, headache, hypertension, hypotension, nausea, vomiting, pain, edema and rash.

**ADVERSE REACTIONS REPORTED:**
- GENERAL DISORDERS
  - Pyrexia, Redness at injection site, nausea vomiting, pain, edema and rash
- HYPERSENSITIVITY
  - Hives, itching, tightness of chest, wheezing
- CARDIOVASCULAR
  - Hypertension, Hypotension

## References:
- Niastase RT® Product Monograph – Date of Approval: November 25, 2015
- Part III Niastase RT® Consumer Information

## Reviewed By:
- Dr. Donald Houston
- Dr. Jayson Stoffman