ALBERTA PRECISION LABORATORIES
Leaders in Laboratory Medicine

NiaStase RT®

APPLICABILITY: This document applies to APL, AHS, Covenant Health, and all other health care professionals involved in the transfusion of blood components and products in Alberta.	***Other Names:*** *recombinant Factor VIIa, eptacog alfa (activated)* ***Company:*** *Novo Nordisk* ***Class:*** *Manufactured recombinant product*

In the event of discrepancy between APL Monograph and Manufacturer's documentation or patient resources, the APL Monograph will take precedence.

	INTRAVENOUS			OTHER		
ROUTES	**DIRECT IV**	**IV Infusion**	**Continuous Infusion**	**SC**	**IM**	**OTHER**
Acceptable Routes*	Yes**	Yes	No	No	No	N/A

DESCRIPTION:

- NiaStase RT® is a white lyophilized powder that contains activated recombinant Factor VII.
- Supplied in 1.0 mg (50KIU), 2.0 mg (100 KIU), and 5.0 mg (250 KIU) single use vials.
- Also contains calcium chloride dehydrate, glyclyglycine, mannitol, methionine, polysorbate 80, sodium chloride, and sucrose. The solvent for reconstitution contains histidine in water for injection.
- Latex-free

AVAILABILITY

- Supplied by Canadian Blood Services.
- Contact your local laboratory/transfusion service regarding stock availability on site.

INDICATIONS FOR USE:

- In Hemophilia A/B patients with inhibitors to Factor VIII or Factor IX, respectively, for the treatment of bleeding episodes (including treatment and prevention of those occurring during and after surgery).
- For treatment of severe bleeding episodes in Glanzmann's thrombasthenia with clinical refractoriness and/or platelet specific antibodies, or where platelets are not immediately available (including treatment of severe bleeding episodes and/or prevention of bleeding in surgical interventions or invasive procedures).
- In adult patients with acquired hemophilia, for the treatment of bleeding episodes, and for the prevention of bleeding in those undergoing surgery or invasive procedures.
- In patients with congenital Factor VII deficiency, for the treatment of bleeding episodes and for the prevention of bleeding in those undergoing surgery or invasive procedures.

CONTRAINDICATIONS:

- Known hypersensitivity to any of the constituents in the preparation of NiaStase®, or to mouse, hamster, or bovine protein.

WARNINGS:

- Both arterial and venous thromboembolic adverse events have been reported after NiaStase® treatment, mostly in patients with predisposing concurrent risk factors.
- Caution should be exercised in: patients with the following conditions: history of coronary heart disease, liver disease, immobilized post-operatively, neonates, risk of thromboembolic phenomena, or disseminated intravascular coagulation (DIC).
- Patients with DIC, advanced atherosclerotic disease, crush injury, septicemia, or concomitant treatment with aPCCs/PCCs (activated/non-activated prothrombin complex concentrates) may have an increased risk of developing thrombotic events due to their underlying condition or concomitant treatment.
- Patients with inherent Factor VII deficiency may have pre-existing or may develop anti-Factor VII antibodies during therapy with NiaStase RT®. The clinical significance of these antibodies is unknown.

DOSE:

- Dose to be determined by the most responsible health practitioner (MHRP).
- Consult with Hematologist or bleeding disorders clinic
- Hemostasis evaluation should be used to determine the effectiveness of NiaStase RT® and to provide a basis for modification of the treatment schedule
- Refer to patient's care plan or Factor First card, if not available consult with bleeding disorders clinic or transfusion medicine physician.

Manufacturer Recommended Dosing:

Indication	Situation	Recommended Dose	Frequency and Duration
Congenital Hemophilia A or B with Inhibitors	Bleeding episodes	90 ug/kg • *Doses between 30 and 120 ug/kg have been used successfully in clinical trials. Both the dose and administration interval may be adjusted based on the severity of the bleeding and degree of hemostasis achieved.*	• Initial dose of 90 ug/kg • Administer every 2 hours until clinical improvement is observed • If continued therapy is required, dosage interval may be increased from 2 to 6 hours
	Surgery	90 ug/kg • *Dose may vary depending on surgery type*	• Initial dose of 90 ug/kg • Administer prior to surgery and at least every 2 hours during the procedure • Repeat dosing every 2 hours for the first 24-48 hours after surgery (depending on surgery performed and clinical status of patient) • Dosing may be repeated once during the 2-hour interval after surgery depending on the clinical status of patient • If continued therapy is required, dosage interval may be increased from 2 to 6 hours
Glanzmann's Thrombasthenia*	Treatment of severe bleeding episodes	90 ug/kg	• A dose of 90 ug/kg repeated every 2-6 hours until hemostasis is achieved • NiaStase RT® can be used alone or in combination with other hemostatic agents (e.g. antifibrinolytics) and/or transfusion of platelets
	Prevention of bleeding during surgery	90 ug/kg • *Higher average infused doses (median dose of 100 ug/kg) were noted for surgical patients who had clinical refractoriness with or without platelet-specific antibodies compared to those with neither.*	• Initial dose of 90 ug/kg given immediately before the intervention and repeated at 2-hour intervals for the duration of the surgery • Post-surgical doses should be administered at 2–6-hour intervals to prevent post-operative bleeding
Acquired Hemophilia	Bleeding Episodes and/or Surgery	90 ug/kg	• Initial dose of 90 ug/kg administered by intravenous bolus injection every 2-3 hours • Once hemostasis has been achieved, the dose interval can be increased successively to every 4, 6, 8 or 12 hours (for as long as treatment is judged to be indicated)

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Indication	Situation	Recommended Dose	Frequency and Duration
Congenital Factor VII Deficiency	Bleeding Episodes	15-30 ug/kg	• Recommended dose range for treatment of bleeding episodes is 15-30 ug/kg every 4-6 hours until hemostasis is achieved

			• Dose and frequency of injections should be adapted to each individual
	Surgery	15-30 ug/kg	• The recommended dose range for the prevention of bleeding in patients undergoing surgery or invasive procedures is 15-30 ug/kg immediately before surgery, repeat every 4-6 hours for the duration of the surgery and until hemostasis is achieved. • Dose and frequency of injections should be adapted to each individual

***** The minimum effective dose for the treatment of bleeding episodes and prevention of bleeding during surgery in Glanzmann's thrombasthenia has not been determined. In patient without refractoriness to platelets or in patients without platelet-specific antibodies platelets are the primary treatment. In these patients, NiaStase RT® should be reserved for treatment when platelets are not immediately or readily available.

ADMINISTRATION:

Confirm written (signed) consent has been obtained and documented prior to requesting blood component from lab/transfusion service where possible.

Pre-Infusion: Ensure recent patient weight is on file and pertinent labs are available. Perform the appropriate pre-transfusion checks per nursing protocol.

Access: Product can be given via CVC, PICC, or peripheral IV line

Reconstitution Supplies:

- NiaStase RT® Product (lyophilized powder)
- 10 mmol/L histidine solvent (prefilled MixPro® syringe* included with product)
- Plunger rod (included with product)
- Vial adapter (included with product)
- Alcohol swabs (not included with product)

Administration Supplies:

- Alcohol swabs
- Sterile plastic luer lock syringe, large enough to contain dose*
- Infusion set (not included with product)

  ***Note:** The pre-filled glass syringe with diluent used to reconstitute and administer product may not be compatible with all needless connectors for intravenous catheters (e.g. ICU Medical MicroClave® Neutral Connector). You may need to withdraw reconstituted product into a sterile 10 mL (or larger) plastic syringe with a standard luer-lock connector. Ensure the vial adapter is used when withdrawing the solution from the vial into the syringe.

Reconstitution:

- See Prefilled Syringe with Vial Adapter Reconstitution Instructions.

Administration:

- Give immediately after reconstitution.
- Do not use solutions that are cloudy, have deposits, or are not colourless
- Intended for IV bolus administration only.
- Do Not mix with other drugs or IV solutions.
- Do Not store reconstituted NiaStase RT® in syringes.
- If administered via a central venous access device, use 0.9 sodium chloride for injection to flush the line after administration, if required.
- Administration rate:
  - Administration rate should be specified by the MRHP after patient assessment.
  - Recommended direct IV administration over a period of 2-5 minutes, depending on the total volume.

NURSING IMPLICATIONS:

Patient Monitoring:

- Vital Signs: Pre-administration, on completion of dose, and as patient condition requires.
- If the patient has experienced previous adverse reaction to product transfusion, or this is the first transfusion of product for patient, monitor for 30-60 minutes post.

Patients receiving blood product transfusions must be observed closely for signs of any unexpected or untoward reactions. These reactions may occur during or after the infusion of blood or blood products. For follow up to a transfusion reaction see Transfusion Reactions | Alberta Health Services. Notify the transfusion service as soon as possible that an adverse reaction has occurred.

Documentation:

- Ensure documentation is completed as per the AHS Transfusion of Blood Components and Products Policy
- Start and stop time of infusion and assessment of patient tolerability should be documented in appropriate flow chart or clinical record (electronic or paper).
- Document vital signs as required in the appropriate flow chart or clinical record (electronic or paper).

Provide patient notification of transfusion documentation where required.

POTENTIAL HAZARDS WITH PARENTERAL ADMINISTRATION:

Adverse Events

- Potential adverse events related to a blood product transfusion range in severity from minor with no sequelae to life-threatening.
- All adverse events occurring during a transfusion should be evaluated to determine whether or not the transfusion can be safely continued/restarted.
- All adverse events suspected to be related to a product transfusion (whether during or after a transfusion) must be reported to your local transfusion service.
- The most serious adverse reaction observed in patients receiving NiaStase RT ® are thrombotic events, however the extent of the risk of thrombotic adverse events after treatment in individuals with congenital hemophilia with inhibitors is considered to be low.
- The most commonly reported adverse reactions in patients receiving NiaStase® are pyrexia, injection site reactions, headache hypertension, hypotension, nausea, vomiting, pain, edema and rash. Monitor for signs and symptoms of thrombosis.

Side Effects - Flushing - Headache - Nausea - Itching and redness at the venipuncture site	→	**Action:** Slow rate of infusion
Potential Allergic Reaction - Stuffy nose - Hives/severe itching - Cough - Chest pain - Wheezing - Facial swelling - Fainting	→	**Action:** **STOP** infusion **IMMEDIATELY** and contact physician

STORAGE & STABILITY OF PRODUCT:

- Stored at 2-25°C.
- Do not freeze.
- Keep protected from light.
- Reconstituted product in its original vial (do not store in syringes) is stable for 6 hours at Room Temperate (<25°C) and 24 hours at refrigerated (2-8°C)
- Do not use expired product.

CONTACT INFORMATION:

Approved By: APL Transfusion Medicine Discipline Council
For questions or comments please contact: Transfusion.SafetyTeam@albertaprecisionlabs.ca

REFERENCES:

NiaStase® Product Monograph. Available from www.novonordisk.ca