Berinert® C1 Esterase Inhibitor (Human)

Class: Manufactured blood product, derived from human plasma

OTHER NAMES: C1 Esterase Inhibitor

Company: CSL Behring

<table>
<thead>
<tr>
<th>ROUTES</th>
<th>DIRECT IV</th>
<th>IV Infusion</th>
<th>Continuous Infusion</th>
<th>SC</th>
<th>IM</th>
<th>OTHER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acceptable Routes*</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes*</td>
<td>No</td>
<td>N/A</td>
</tr>
</tbody>
</table>

*Subcutaneous administration is currently considered off-label use and may only occur at the direction of the Rare Blood Disorders/Angioedema Clinic physician.

Professionals performing these restricted activities have received authorization from their regulatory college and have the knowledge and skill to perform the skill competently.

DESCRIPTION OF PRODUCT:

- Lyophilized, human plasma-derived concentrate of C1 esterase inhibitor (C1-INH)
- Viral inactivation steps include pasteurization, nanofiltration and chromatography as well as screening of the plasma donors.
- Available in 2 dose sizes: Berinert® 500 contains 500 IU C1-INH with 10 mL diluent (sterile water for injection), and Berinert® 1500 (volume reduced) contains 1500 IU C1-INH (volume reduced) with 3 mL sterile water for injection.
- Clinically relevant non-medicinal ingredients include: glycerin, sodium chloride and sodium citrate.
- Latex-free

AVAILABILITY:

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

INDICATIONS FOR USE:

- For the treatment of acute abdominal, laryngeal or facial attacks of hereditary angioedema (HAE) in adult and adolescent patients

CONTRAINDICATIONS:

- Patients who have experienced life-threatening hypersensitivity reactions, including anaphylaxis, to C1-INH preparations

WARNINGS:

- Hypersensitivity reactions may occur. Immediate access to epinephrine is required to treat any acute severe hypersensitivity following discontinuation of administration.
- Thrombotic events have occurred in patients receiving high off-label dosing.

DOSE (Refer to Product Insert):

- Recommended dose: 20 units/kg body weight. Consult Hematologist or bleeding disorders clinic.

ADMINISTRATION:

Ensure patient consent has been obtained prior to requesting blood product from lab/transfusion service where possible.

Pre-Infusion: Ensure recent patient weight and height is on file. Perform the appropriate pre-transfusion checks per protocol.

Access: Berinert® can be given via CVC, PICC or Port-a-Cath®. Subcutaneous administration may be performed at the direction of a Hematologist or the bleeding disorders clinic physician.
### Reconstitution Supplies:
- Vial of Berinert® lyophilized powder
- Vial of Sterile Water for Injection (diluent)
- Mix2Vial™ transfer device

### Administration Supplies:
- **For direct IV or subcutaneous administration:**
  - Sterile plastic Luer lock syringe (large enough to contain dose)

### Reconstitution:
Bring Berinert® vial(s) and diluent vial(s) to room temperature.

Berinert® uses the Mix2Vial™ device for reconstitution.
- Directions on the use of the device can be found at: [http://www.albertahealthservices.ca/assets/wf/lab/wf-lab-clin-tm-mix2vial-reconst-inst.pdf](http://www.albertahealthservices.ca/assets/wf/lab/wf-lab-clin-tm-mix2vial-reconst-inst.pdf).
- If the vacuum is lost, troubleshooting guide can be found at: [http://www.albertahealthservices.ca/assets/wf/lab/wf-lab-clin-tm-mix2vial-troubleshoot.pdf](http://www.albertahealthservices.ca/assets/wf/lab/wf-lab-clin-tm-mix2vial-troubleshoot.pdf).

### Administration:
- Give within 30-60 minutes of reconstitution. **DO NOT** refrigerate after reconstitution.
- Separate line infusion is recommended. **DO NOT** mix with any other medications or other solutions.
- Discard any unused portions within 8 hours.
- **Administration rate:** Slow Direct IV at 4 mL/min. Consult with Hematologist or bleeding disorders clinic for subcutaneous infusion rates.

### NURSING IMPLICATIONS:

**Precautions During Use:**
- Assess vital signs pre and post infusion, and as patient condition requires.

**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 transfusion reaction instructions, refer to: [http://www.albertahealthservices.ca/lab/page4240.aspx](http://www.albertahealthservices.ca/lab/page4240.aspx)

**Documentation:**
- Ensure documentation is completed as per the AHS Transfusion of Blood Components Products procedure.
- Document start and stop time of infusion and patient tolerability should be documented in appropriate flow chart or clinical record (electronic or paper) as required.
- Recipients of blood products are to be notified in writing of the transfusion.
POTENTIAL HAZARDS WITH PARENTERAL ADMINISTRATION:

- 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) should be reported to your local transfusion service.
- Most serious adverse reaction reported in subjects enrolled in clinical studies was an increase in the severity of pain associated with HAE. Most common were subsequent HAE attacks, headache, abdominal pain, nausea, muscle spasm, pain, diarrhea and vomiting.
- Severe hypersensitivity reactions may also occur. Epinephrine should be immediately available for treatment. Signs or symptoms may include hives, generalized urticaria, tightness of chest, wheezing, hypotension, and/or anaphylaxis during or after injection.
- Thrombotic events have been reported when used off-label and at higher then labeled doses.

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<tr>
<th>Side Effects</th>
<th>Action</th>
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<tbody>
<tr>
<td>- Flushing</td>
<td>Slow rate of infusion</td>
</tr>
<tr>
<td>- Headache</td>
<td></td>
</tr>
<tr>
<td>- Nausea</td>
<td></td>
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<tr>
<td>- Itching and redness at the venipuncture site</td>
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<tr>
<th>Potential Allergic Reaction</th>
<th>Action</th>
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<tr>
<td>- Stuffy nose</td>
<td>STOP infusion IMMEDIATELY</td>
</tr>
<tr>
<td>- Hives/severe itching</td>
<td>and contact physician</td>
</tr>
<tr>
<td>- Cough</td>
<td></td>
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<tr>
<td>- Chest pain</td>
<td></td>
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<tr>
<td>- Wheezing</td>
<td></td>
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<tr>
<td>- Facial swelling</td>
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<td>- Fainting</td>
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STORAGE & STABILITY of PRODUCT:

- Store at 2-25 °C. DO NOT freeze
- Keep vials in storage box until use. Protect from light.
- Product expires 30 month (Berinert® 1500) and 36 months (Berinert® 500) from date of manufacture. Expiration date is indicated on package.

COMMENTS:
Date Effective: 12 Aug. 2016
Revised Date: 14 Jul. 2016
Version: 1.3
Document Number: PTMGNR00026
Approved By: TM Network
Questions or concerns with this document can be addressed to transfusion.safetyteamn@ahs.ca

REFERENCES
BERINERT® Product monograph SCN 174757
Inmaculada Martinez-Saguer, Marco Cicardi, Chiara Suffritti, Eva Rusicke, Emel Aygören-Pürsün, Hildegard Stoll, Tanja Rossmanith, Annette Feussner, Uwe Kalina, and Wolfhart Kreuz. Pharmacokinetics of plasma-derived C1-esterase inhibitor after subcutaneous versus intravenous administration in subjects with mild or moderate hereditary angioedema: the PASSION study. Transfusion 2014:54:1552-1561
http://www.cslbehring.ca