FROSTBITE PROTOCOL

Rapid rewarming of extremities in hot water (39°C) with chlorhexidine and isopropyl alcohol for 30 minutes

Assessment of severity (Grade 1-4) (see figure below)
Documentate severity for comparison after therapy
(Use “Quantification of Frostbite Injury” sheet)

Grade 1
Hydrotherapy whirlpool daily
Debridement and aspiration of clear blisters
Aloe vera and Mepitel dressing
Elevation of affected parts
Avoid tobacco and alcohol
Tetanus-diphtheria immunization

Grade 2-3
If less than 72 hours since rewarming:
Management as per Grade 1 + Illoprost intravenous infusion for 6 hours for 5 days

Grade 4
If less than 72 hours since rewarming:
Management as per Grade 1 + Illoprost intravenous infusion for 6 hours for 5 days
If less than 24 hours since rewarming:
Add:
Alteplase intravenous infusion once and Frostbite Heparin Protocol intravenous infusion for 72 hours (see page 3 of Pre-Printed Orders)

You may consult Dr. Alex Poole and Clinical Pharmacist Josianne Gauthier for guidance

FROSTBITE PROTOCOL

PHYSICIAN’S PRE-PRINTED ORDERS (Page 1 of 3)

DATE: ___________________ TIME: ___________________ PATIENT ACTUAL WEIGHT: ___________________

* This is a protocol using a Special Access Program drug and off-label indication. For Adults only. Review medications precautions, contraindications and administration instructions *

GRADE 1-4

- Treatment of hypothermia and/or severe trauma takes priority
- Remove jewelry or other extraneous material from the body part
- As soon as possible, initiate rapid re-warming of frostbite parts in water 39°C with chlorhexidine gluconate 2%/isopropyl alcohol 4% (Stanhexidine) (30 mL per liter) until area becomes soft and pliable (30 minutes)
- Let skin air dry, do not rub. Protect from direct trauma
- Consult surgery for aspiration of clear blisters and for further wound care during hospital admission
- Elevate affected parts and avoid ambulation on thawed lower extremity (unless only distal toes affected)
- Encourage oral hydration or start warm IV normal saline boluses ________ mL/hour
- Tetanus-diphtheria (Td) adsorbed 0.5 mL intraMUSCULAR once
- Consult therapies for contractures and splinting
- Avoid tobacco and alcohol
- Apply Mepitel dressing Daily (after rewarming/hydrotherapy and physician/surgeon assessment completed)
- Starting the day after rewarming (if applicable), immerse affected digits in warm tap water once daily for 30 minutes using the hydrotherapy portable whirlpool if available (use basin or tub if not available) (no chlorhexidine required)

MEDICATIONS

☐ Aloe Vera (Aloe Vesta Protective ointment) Apply topically on frostbitten parts Daily
☐ Ibuprofen 600 mg oral every 6 hours (Do NOT give if alteplase and heparin ordered)
☐ Morphine 5 – 10 mg oral every 4 hours as needed for pain or
☐ Morphine 2 – 4 mg intraVENOUS every 2 hours as needed for pain
☐ Pantoprazole 40 mg oral or intravenous once daily

GRADE 2 OR MORE

☐ CBC, Electrolytes, PTT, INR, Type and Screen for 2 units
☐ Ensure staffing available to monitor patient every 15 minutes for 2 hours then every 30 minutes for 6 hours
☐ ILOPROST intraVENOUS INFUSION (refer to “Iloprost Administration Instructions” sheet)
- Obtain 1 ampoule of iloprost 50 mcg (0.5 mL) from pharmacy or Night cupboard
- Dilute 50 mcg (0.5 mL) in Dextrose 5% (D5W) 250 mL bag for a final concentration of 0.2 mcg/mL
  *Requires an independent double-check _____/_____
- Physician must be readily available following the initiation of the infusion or dosage increase (on Day 1 only)
- Start intraVENOUS infusion at 10 mL/hour and increase infusion rate by 10 mL/hour every 30 minutes to a maximum of
  ☐ 30 mL/hour for patients 40-50 kg ☐ 40 mL/hour for patients 51-74 kg ☐ 50 mL/hour for patients 75 kg or more
- Continue infusion for a maximum of 6 hours (regardless of rate of administration). For patients 75 kg or more, do not exceed one bag. Repeat infusion daily for a total of 5 days
- Measure blood pressure and heart rate every 15 minutes for 2 hours then every 30 minutes
- If headaches, tachycardia (heart rate > 100 beats/minute), palpitations, hypotension (systolic blood pressure < 90 mmHg), nausea, vomiting or facial flushing, decrease the infusion rate by 10 mL/hour and re-assess 30 minutes later (these are dose-related side effects; usually quickly disappear with dose reduction)
- If patient tolerates infusion well on Day 1 and 2, may initiate infusion at maximum infusion rate on Day 3, 4 and 5
- This is a Special Access Program drug requiring documentation on SAP form (Notify pharmacist)

PHYSICIAN’S NAME: _____________________________ PHYSICIAN’S SIGNATURE: ____________________________

Approved by P&T: April 16, 2018
Approved by MAC: April 18, 2018

FAX TO PHARMACY
FROSTBITE PROTOCOL
PHYSICIAN’S PRE-PRINTED ORDERS (Page 2 of 3)

DATE: ___________________________ TIME: ___________________________ PATIENT ACTUAL WEIGHT: _______________

GRADE 4 (IF LESS THAN 24 HOURS SINCE REWARMING)
• Within first hour of iloprost infusion, initiate:
  □ ALTEPLASE intraVENOUS INFUSION

<table>
<thead>
<tr>
<th>Time</th>
<th>Initials</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<tr>
<td></td>
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</tbody>
</table>

Give ________ mg (recommended 0.15 mg/kg) intraVENOUS over 15 minutes
then ________ mg/hour (recommended 0.15 mg/kg/hour) intraVENOUS for 6 hours then discontinue (i.e. Day 1 only) Total maximum dose (including bolus) = 100 mg

• Alteplase must be initiated as soon as possible within 24 hours of rewarming
• See contraindications below and administration instructions on reverse (dilute to final concentration of 1 mg/mL)
• Start Frostbite Heparin Protocol within 1 hour of starting alteplase infusion

THROMBOLYTIC THERAPY

<table>
<thead>
<tr>
<th>ABSOLUTE CONTRAINDICATIONS</th>
<th>RELATIVE CONTRAINDICATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Do not use if any of the following are present)</td>
<td></td>
</tr>
<tr>
<td>• History of any intracranial hemorrhage</td>
<td>• History of chronic, severe, poorly controlled hypertension</td>
</tr>
<tr>
<td>• History of ischemic stroke within the preceding three months (exception: acute ischemic stroke within 4.5 hours, treated with thrombolytic therapy)</td>
<td>• Uncontrolled hypertension at presentation (blood pressure greater than 180 mmHg systolic and/or 110 mmHg diastolic)</td>
</tr>
<tr>
<td>• Presence of a cerebral vascular malformation</td>
<td>• History of ischemic stroke more than three months previously</td>
</tr>
<tr>
<td>• Known primary or metastatic intracranial malignancy</td>
<td>• Dementia</td>
</tr>
<tr>
<td>• Symptoms or signs suggestive of an aortic dissection</td>
<td>• Traumatic or prolonged (&gt;10 min) CPR</td>
</tr>
<tr>
<td>• A bleeding diathesis or active bleeding, with the exception of menses</td>
<td>• Any known intracranial disease that is not an absolute contraindication</td>
</tr>
<tr>
<td>• Significant closed-head or facial trauma within the preceding three months</td>
<td>• Major surgery within the preceding three weeks</td>
</tr>
<tr>
<td>• Intracranial or intraspinal surgery within 2 months</td>
<td>• Recent (2 to 4 weeks) internal bleeding</td>
</tr>
<tr>
<td>• Uncontrolled hypertension at presentation (unresponsive to emergency treatment)</td>
<td>• Active peptic ulcer</td>
</tr>
<tr>
<td></td>
<td>• Noncompressible vascular punctures</td>
</tr>
<tr>
<td></td>
<td>• Pregnancy</td>
</tr>
<tr>
<td></td>
<td>• Current use of anticoagulants</td>
</tr>
</tbody>
</table>

PHYSICIAN’S NAME: ___________________________ PHYSICIAN’S SIGNATURE: ___________________________
GRADE 4 (IF ALTEPLASE GIVEN)

- **HEPARIN BOLUS AND INITIAL INFUSION** (Frostbite Protocol Heparin)
  - Start heparin within 1 hour of starting alteplase infusion
  - Administer bolus using heparin 1000 units/mL (10 mL) vial then initiate infusion using heparin 25 000 units (50 units/mL) in Dextrose 5% 500 mL pre-mixed bag per chart below. Indicate time and initials
  - Then adjust heparin infusion based on PTT results. Document bolus and adjustments on Heparin Infusion Flowsheet

<table>
<thead>
<tr>
<th>Time</th>
<th>Initials</th>
</tr>
</thead>
<tbody>
<tr>
<td>/</td>
<td>/</td>
</tr>
</tbody>
</table>

Heparin infusion adjustment

- Measure PTT 6 hours after initial bolus then adjust heparin per chart below for **24 hours**

<table>
<thead>
<tr>
<th>Patients</th>
<th>Dose change</th>
<th>PTT &lt; 36 sec</th>
<th>PTT 36-45 sec</th>
<th>PTT 46-60 sec</th>
<th>PTT 61 sec or greater</th>
</tr>
</thead>
<tbody>
<tr>
<td>26 – 35</td>
<td>↑ 2 mL/hour</td>
<td>2400 units</td>
<td>1200 units</td>
<td>1200 units</td>
<td>Therapeutic – No dose change</td>
</tr>
<tr>
<td>36 - 45</td>
<td>↑ 3 mL/hour</td>
<td>3200 units</td>
<td>1600 units</td>
<td>1600 units</td>
<td></td>
</tr>
<tr>
<td>46 – 55</td>
<td>↑ 4 mL/hour</td>
<td>4000 units</td>
<td>2000 units</td>
<td>2000 units</td>
<td></td>
</tr>
<tr>
<td>56 – 65</td>
<td>↑ 5 mL/hour</td>
<td>4800 units</td>
<td>2400 units</td>
<td>2400 units</td>
<td></td>
</tr>
<tr>
<td>66 – 75</td>
<td>↑ 6 mL/hour</td>
<td>5600 units</td>
<td>2800 units</td>
<td>2800 units</td>
<td></td>
</tr>
<tr>
<td>76 – 85</td>
<td>↑ 7 mL/hour</td>
<td>6400 units</td>
<td>3200 units</td>
<td>3200 units</td>
<td></td>
</tr>
<tr>
<td>86 – 95</td>
<td>↑ 8 mL/hour</td>
<td>7200 units</td>
<td>3600 units</td>
<td>3600 units</td>
<td></td>
</tr>
<tr>
<td>96 – 105</td>
<td>↑ 9 mL/hour</td>
<td>8000 units</td>
<td>4000 units</td>
<td>4000 units</td>
<td></td>
</tr>
<tr>
<td>106 – 115</td>
<td>↑ 10 mL/hour</td>
<td>8800 units</td>
<td>4400 units</td>
<td>4000 units</td>
<td></td>
</tr>
</tbody>
</table>

**NEXT PTT DUE**

- IN 6-8 HRS
- IN 6-8 HRS
- IN 6-8 HRS

After 24 hours, use Standard Heparin Protocol for an additional 48 hours (obtain new orders)

**PHYSICIAN’S NAME:** _____________________________  **PHYSICIAN’S SIGNATURE:** _____________________________  **FAX TO PHARMACY**

Approved by P&T: April 16, 2018  Approved by MAC: April 18, 2018
FROSTBITE PROTOCOL
QUANTIFICATION OF FROSTBITE INJURY

DATE: _____________________ TIME: _____________________

- Mark with a dark pen the extent of the injury. Note skin changes such as clear blisters or hemorrhagic blisters.
- This sheet can also be used to monitor progress and change.

Left

Right

Left

Right

PHYSICIAN’S NAME: _____________________________ PHYSICIAN’S SIGNATURE: _________________________________________
# FROSTBITE PROTOCOL

## SUPPLEMENTAL INFORMATION

### Iloprost contraindications

- Pregnancy, lactation
- Conditions where the effect of iloprost on platelets might increase risk of hemorrhage (e.g. active peptic ulcers, trauma, intracranial hemorrhage)
- Severe coronary heart disease or unstable angina
- Myocardial infarction within the last 6 months
- Acute or chronic congestive heart failure (NYHA II-IV)
- Severe arrhythmias
- Suspected pulmonary congestion

### Iloprost special precautions

- Surgery should not be delayed in patients requiring urgent amputation (e.g. in infected gangrene)
- Iloprost elimination is reduced in patients with hepatic dysfunction and in patients with renal failure requiring dialysis
- In patients with low blood pressure care should be taken to avoid further hypotension and patients with significant heart disease should be closely monitored
- Monitor for possible orthostatic hypotension in patients getting up from the lying to an upright position after the end of administration
- For patients with a cerebrovascular event (e.g. transient ischemic attack, stroke) within the last 3 months a careful benefit-risk evaluation should be undertaken
- Currently only sporadic reports of use in children and adolescents are available
- The paravascular infusion of undiluted iloprost can lead to local changes at the injection site
- Oral ingestion and contact with mucous membranes must be avoided. On contact with the skin, iloprost may provoke long-lasting erythema

Reference: Schering Company Core Data Sheet (provided by Bayer December 2014)
ILOPROST (ILOMEDIN) ADMINISTRATION INSTRUCTIONS

Classification: Prostaglandin Analogue  
Alternate name(s): Ilomedin  
Last Reviewed: January 16 2015

Indications/Ordering Restrictions (iloprost)

- Special Access Program Drug
- Authorized for use by Dr. Alex Poole (or in consultation with Dr. Poole) for severe frostbite ONLY

Reconstitution & Stability (iloprost)

- Ampoules are stored at room temperature
- Each 0.5 mL ampoule contains 50 microgram of iloprost (as iloprost trometamol)
- Dilute 50 mcg (0.5 mL) in Dextrose 5% (D5W) 250 mL bag for a final concentration of 0.2 mcg/mL
- Reconstituted solution is stable at room temperature for 24 hours

Compatibility (iloprost)

- Compatible with sodium chloride 0.9% (Normal Saline) and D5W
- Do not mix with other drugs; compatibility unknown

Administration (iloprost)

- Administration restricted to Critical Care Units or under close hemodynamic monitoring
- Anaphylaxis precautions: have diphenhydramine, epinephrine and hydrocortisone at the bedside
- Physician must be readily available for at least 10 minutes following the initiation of any infusion or dosage increase
- Do not handle if pregnant or breastfeeding

Dosage (iloprost)

- Dose range: 0.5 to 2 nanogram/kg/min
- For severe frostbite, using diluted solution of 0.2 mcg/mL, start intraVEOUS infusion at 10 mL/hour and increase rate by 10 mL/hour every 30 minutes to a maximum of
  - 30 mL/hour for patients 40-50 kg
  - 40 mL/hour for patients 51-74 kg
  - 50 mL/hour for patients 75 kg or more
- Rate is adjusted to individual tolerability. If headaches, hypotension, tachycardia, palpitations, nausea, vomiting or facial flushing, decrease the infusion rate by 10 mL/hour and re-assess 30 minutes later (these are dose-related side effects; usually quickly disappear with dose reduction)
- Continue infusion for 6 hours and repeat infusion daily for 5 days
- If patient tolerates infusion well on Day 1, 2 and 3, may initiate infusion at maximum infusion rate on Day 4 and 5
Potential Hazards of Parenteral Administration (iloprost)

- LOCAL SITE REACTIONS: redness and pain at the injection site
- Oral ingestion and contact with mucous membrane must be avoided. On contact with the skin, iloprost may provoke long-lasting erythema
- OTHER: allergic reactions

Important Implications (iloprost)

Side Effects Include:
- MOST COMMON: headache, facial flushing, nausea and vomiting. These are dose related, often at the start of treatment during titration and usually disappear quickly with dose reduction
- OTHER: dizziness, tingling or burning sensation, bradycardia, hypotension, diarrhea, abdominal pain, myalgias or arthralgias
- See POTENTIAL HAZARDS OF PARENTERAL ADMINISTRATION

Monitoring Parameters Include:
- Baseline blood pressure and heart rate every 15 minutes for 2 hours then every 30 minutes
- The possibility of orthostatic hypotension should be borne in mind in patients getting up from the lying to an upright position after the end of administration

Contraindications/cautions Include:
- There is a potential for increased risk of bleeding when given to patients on warfarin, heparin or platelet inhibitors like ASA or non-steroidal anti-inflammatory agents
- There is a potential for increased risk of bleeding in patients at risk of hemorrhage (e.g. active peptic ulcers, trauma, intracranial hemorrhage)
- Contraindicated in pregnant or breastfeeding women, patients with unstable angina, severe coronary heart disease, myocardial infarction within the last 6 months, acute or chronic congestive heart failure (NYHA II-IV), severe arrhythmias or suspected pulmonary congestion

Other:
- Dosage reduction is required in patients with severe liver or renal disease
- ELDERS ALERT: Cases of acute pulmonary edema or heart failure in the elderly with advanced arteriosclerosis have been reported

References

1) Winnipeg Regional Health Authority Iloprost trometamol Adult Parenteral Drug Monograph
2) Ilomedin Package Insert. Bayer HealthCare
3) Schering Ilomedin Company Core Data Sheet (obtained from Bayer HealthCare December 2014)
Alteplase Preparation and Administration Instructions

1. Add 100 mL sterile water (provided by the manufacturer) to each 100 mg vial, as per manufacturer’s directions. **Reconstituted concentration: 1mg/mL**

   **Note:** mixing should be done with gentle swirling and/or slow inversion. Avoid excessive or vigorous shaking as this can cause significant foaming. Slight foaming is not unusual and allowing the vial to stand undisturbed for several minutes is usually required.

2. Withdraw alteplase bolus dose into a syringe

3. Administer alteplase bolus dose over 15 minutes intraVENOUS then immediately start alteplase infusion

4. Transfer required volume to an empty 100 mL mini-bag and hang using continu flow with no ports tubing.

5. Connect alteplase infusion tubing to IV Y Site port closest to patient (Compatible with Normal Saline and D5W)

6. Initiate infusion via IV pump.

7. At completion of infusion, stop the alteplase infusion and disconnect from IV Y site. **Do not infuse any drug remaining in the tubing**