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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)
Documentation of 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
Ibuprofen every 6 hours
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
+
Iloprost intravenous infusion for 6 hours for 5 days

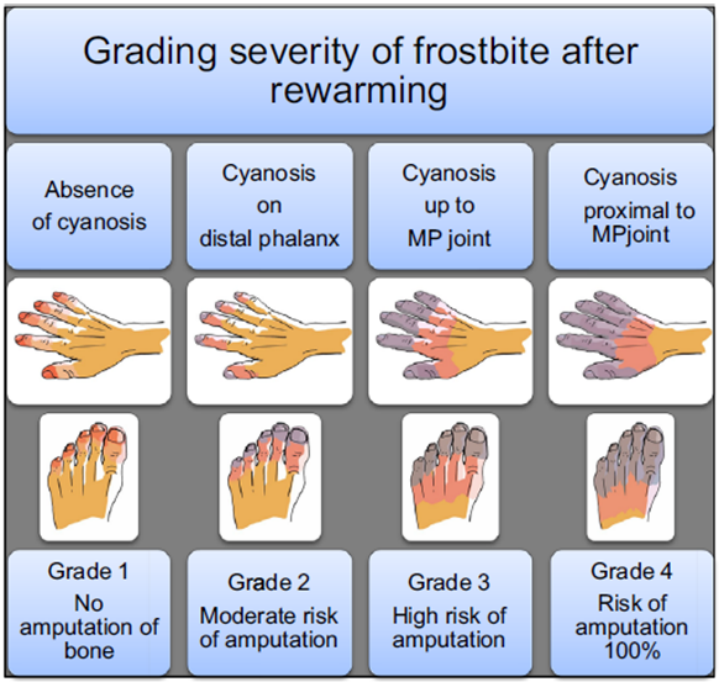
Grade 4

If less than 72 hours since rewarming:

Management as per Grade 1
+
Iloprost intravenous infusion for 6 hours for 5 days

If less than 24 hours since rewarming:

Add:
Alteplase intravenous infusion <u>once</u>
and
Enoxaparin for 72 hours



Source: Cauchy E. et al, Wild & Env Med 27, 92-99 (2016)

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

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PATIENT LABEL

FROSTBITE PROTOCOL
PHYSICIAN'S PRE-PRINTED ORDERS

***** PATIENT'S ACTUAL WEIGHT: _____________ *****

Transcribe each order indicating:
MAR = Medication Administration Record
NCP = Nursing Care Plan
MT = Meditech
Req = Requisition completed

Transcriber | Verifier

*** 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

	Time	Initials
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 in portable whirlpool) 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 enoxaparin ordered**)
☐ Morphine 5 – 10 mg oral every 4 hours as needed for pain
☐ Morphine 2 – 5 mg intraVENOUS every 2 hours as needed for pain
☐ Fentanyl 25 – 50 mcg every 5 minutes as needed for pain (maximum 150 mcg/hour)
☐ Pantoprazole 40 mg oral or intravenous once daily

GRADE 2 – 4

- CBC, Electrolytes, BUN/Creat, PTT, INR
- 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 _____/______
- 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 until *at least* 1 bag given and for a *minimum* of 6 hours. Mix an additional bag as needed.**
- **Repeat infusion daily for a total of 5 days. Consult pharmacist for administration times**
- 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)

DATE: ______________________________ **TIME:** ______________________________

PHYSICIAN'S NAME: ______________________________ **PHYSICIAN'S SIGNATURE:** ______________________________

PATIENT LABEL

FROSTBITE PROTOCOL
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GRADE 4 (IF LESS THAN 24 HOURS SINCE REWARMING)

- Initiate alteplase **as soon as possible** within 24 hours of rewarming

☐ **ALTEPLASE intraVENOUS INFUSION (*requires independent double-check*)**	**Time**	**Initials**
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		/

- See contraindications below and "Alteplase Preparation and Administration Instructions" sheet (dilute to final concentration of 1 mg/mL)
- **Give enoxaparin within 30 minutes of starting alteplase infusion**
- **Blood type and screen**

THROMBOLYTIC THERAPY

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

DATE: ______________________ **TIME:** ______________________

PHYSICIAN'S NAME: ______________________ **PHYSICIAN'S SIGNATURE:** ______________________

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GRADE 4 (IF ALTEPLASE GIVEN)

- **Within 30 minutes of alteplase infusion, initiate enoxaparin:**

eGFR 30 mL/min OR GREATER:

LESS THAN 75 years of age:

☐ Enoxaparin 30 mg intraVENOUS bolus ONCE AND
☐ Enoxaparin __________ (1 mg/kg) subCUTANEOUS every 12 hours for 72 hours. Administer the first subcutaneous dose with the intravenous bolus

GREATER OR EQUAL TO 75 years of age:

☐ Enoxaparin __________ (0.75 mg/kg) subCUTANEOUS every 12 hours for 72 hours

eGFR LESS THAN 30 mL/min:

LESS THAN 75 years of age:

☐ Enoxaparin 30 mg intraVENOUS bolus ONCE AND
☐ Enoxaparin __________ (1 mg/kg) subCUTANEOUS every 24 hours for 72 hours. Administer the First subcutaneous dose with the intravenous bolus

GREATER OR EQUAL TO 75 years of age:

☐ Enoxaparin __________ (1 mg/kg) subCUTANEOUS every 24 hours for 72 hours.

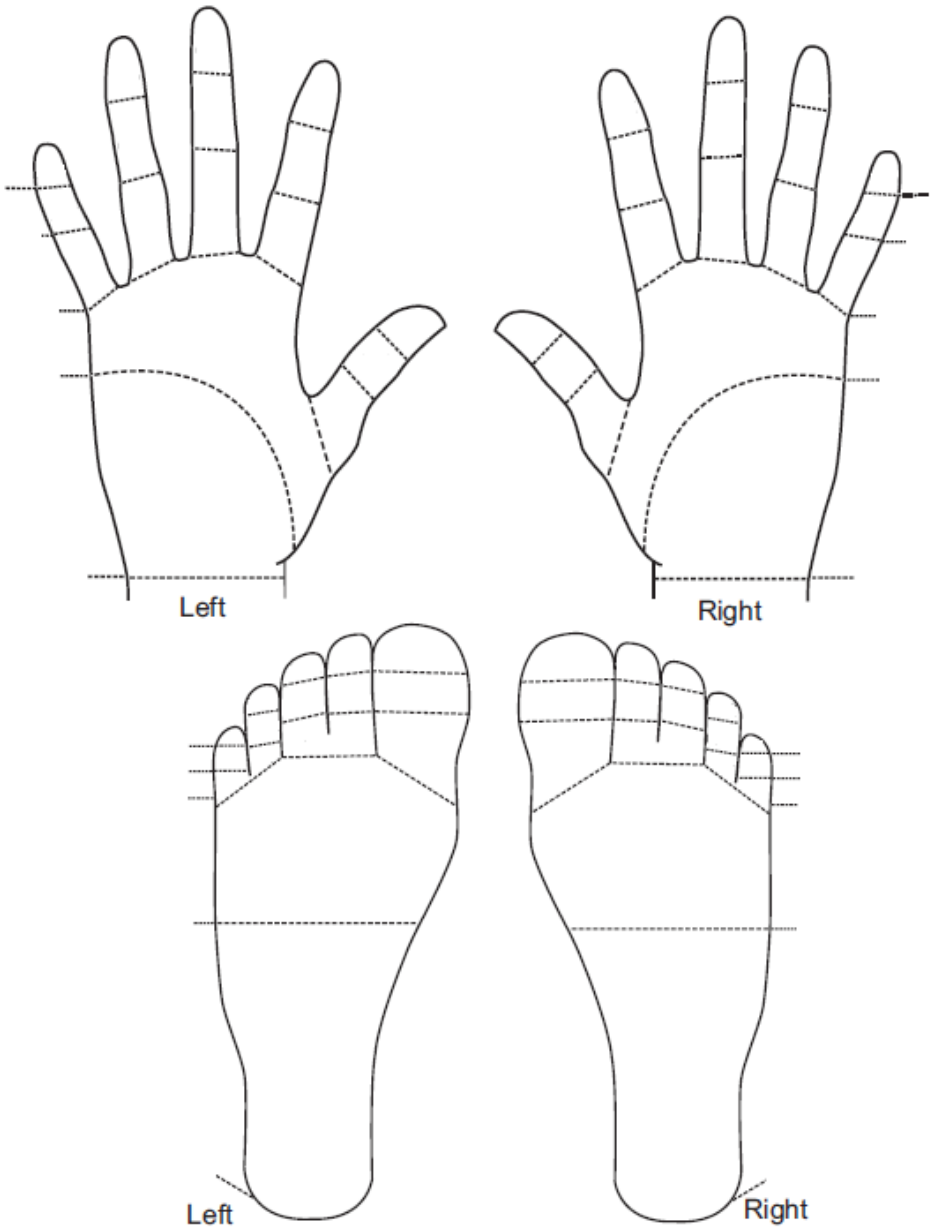
DATE: ______________________ **TIME:** ______________________

PHYSICIAN'S NAME: ______________________ **PHYSICIAN'S SIGNATURE:** ______________________

PATIENT LABEL

FROSTBITE PROTOCOL
QUANTIFICATION OF FROSTBITE INJURY

- Mark with a dark pen the extent of the injury after rewarming. Note skin changes and indicate any evidence of cyanosis and hemorrhagic blisters.
- This sheet can also be used to monitor progress and change



DATE: _____ **TIME:** _____

PHYSICIAN'S NAME: _____ **PHYSICIAN'S SIGNATURE:** _____

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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

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:** December 2020

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
- 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 intraVENOUS 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 until *at least* 1 bag given and for a *minimum* of 6 hours. Mix an additional bag as needed.
- Repeat infusion daily for a total of 5 days. Consult pharmacist for administration times
- If patient tolerates infusion well on Day 1 and 2, may initiate infusion at maximum infusion rate on Day 3, 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) or severe arrhythmias

Other:

- Dosage reduction is required in patients with severe liver or renal disease
- ELDERS ALERT: Cases of acute pulmonary edema or heart failure I 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)

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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**: **1 mg/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. Hang reconstituted alteplase bottle using continu flow with no ports tubing.

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

4. Set pump to infuse bolus dose over 15 minutes. Independent double-check required.

5. Once bolus completed, reprogram the pump to infuse at prescribed rate for 6 hours. Independent double-check required.

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