

Appendix 1 (as submitted by the authors):**DEEP FROSTBITE PROTOCOL***** FOR ADULTS ONLY ***

DATE: _____ TIME: _____ PATIENT ACTUAL WEIGHT: _____

ALLERGIES: _____

*** This is a protocol using a Special Access Program drug and off-label indication.****See medications precautions and contraindications on reverse ***

- Admit to ICU and consult Dr. Poole and Clinical Pharmacist Josianne Gauthier (Pharmacist on-call after pharmacy hours)
- Treatment of hypothermia and/or severe trauma takes priority
- Remove jewelry or other extraneous material from the body part
- Rapid re-warming of frostbite parts in 1000 mL of water 39 degrees Celsius with 30 mL of chlorexidine gluconate 2%/isopropyl alcohol 4% (Stanhexidine) until area becomes soft and pliable to the touch (30 minutes)
- Let skin air dry, do not rub. Protect from direct trauma
- Surgeon to debride and aspirate clear blisters (leave hemorrhagic blisters intact)
- Apply Aloe Vesta Protective ointment and Mepitel dressing Daily
- Elevate affected parts and avoid ambulation on thawed lower extremity (unless only distal toes are affected)
- Encourage oral hydration or start warm IV normal saline boluses _____ mL/hour
- Avoid tobacco and alcohol
- Tetanus-diphtheria (Td) adsorbed 0.5 mL intraMUSCULAR once
- Consult therapies
- Immerse affected digits in hot tap water (39 degrees Celsius) once daily for 30 minutes using the hydrotherapy portable whirlpool (starting the day after re-warming)

MEDICATIONS

- Ibuprofen _____ mg oral every 6 hours (Recommended 12 mg/kg/day to a maximum of 2400 mg/day)
- Morphine 5 – 10 mg oral every 4 hours as needed for pain or
- Morphine 2 – 4 mg intraVENOUS every 4 hours as needed for pain
- ILOPROST intraVENOUS INFUSION (refer to IV monograph with package)**
 - Obtain 1 ampoule of iloprost 50 mcg/mL (0.5 mL) from pharmacy or Nightcupboard
 - 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 for at least 10 minutes following the initiation of any infusion or dosage increase
 - 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**
 - 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)
 - **Repeat infusion daily for 5 days**
 - 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: January 5 2015 / Approved by MAC and Ethics Committee: February 5 2015

Appendix to: Poole A, Gauthier J. Treatment of severe frostbite with iloprost in northern Canada.

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ALLERGIES: _____

ALTEPLASE intraVENOUS INFUSION

- Alteplase must be initiated within 24 hours of rewarming (Day 1 only)
- Using the 50 mg/mL vial, reconstitute alteplase per instructions on reverse to a **final concentration of 1 mg/mL**
- Administer bolus, initial infusion and subsequent infusion per patient weight and chart below. Indicate time and initials
- See contraindications and administration instructions on reverse

	Time	Initials
Alteplase 15 mg intraVENOUS bolus over 2 minutes then		/
Alteplase 0.75 mg/kg intraVENOUS infusion over 30 minutes (max 50 mg) then		/
Alteplase 0.5 mg/kg intraVENOUS infusion over 60 minutes (max 35 mg)		/

Patient weight (kg)	Bolus (mg)	Initial Infusion (over 30 minutes)			Subsequent Infusion (over 60 minutes)		
		Infusion dose (mg)	Infusion rate (mL/hour)	Volume to be infused (mL)	Infusion dose (mg)	Infusion rate (mL/hour)	Volume to be infused (mL)
<input type="checkbox"/> 41 to 42	15	31	62	31	21	21	21
<input type="checkbox"/> 43 to 44	15	32	64	32	22	22	22
<input type="checkbox"/> 45 to 47	15	34	68	34	23	23	23
<input type="checkbox"/> 48 to 49	15	36	72	36	24	24	24
<input type="checkbox"/> 50 to 51	15	38	76	38	25	25	25
<input type="checkbox"/> 52 to 54	15	39	78	39	26	26	26
<input type="checkbox"/> 55 to 56	15	41	82	41	27	27	27
<input type="checkbox"/> 57 to 58	15	43	86	43	28	28	28
<input type="checkbox"/> 59 to 60	15	44	88	44	29	29	29
<input type="checkbox"/> 61 to 63	15	46	92	46	30	30	30
<input type="checkbox"/> 64 to 65	15	48	96	48	32	32	32
<input type="checkbox"/> 66 to 67	15	50	100	50	33	33	33
<input type="checkbox"/> > 67	15	50	100	50	35	35	35

- Start heparin within 1 hour of starting alteplase infusion

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HEPARIN BOLUS AND INITIAL INFUSION

- Give Heparin concurrently with alteplase
- 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

	Time	Initials
Heparin 60 units/kg intraVENOUS bolus STAT (max 4 000 units, rounded to nearest 500 units) then		/
Heparin 12 unit/kg/hour intraVENOUS initial infusion for 6 hours		/

Patient weight (kg)	Bolus (units)	Initial Infusion	
		Infusion dose (units)	Infusion rate (mL/hour)
<input type="checkbox"/> 50 or less	3000	600	12
<input type="checkbox"/> 51 to 61	3500	700	14
<input type="checkbox"/> 62 to 73	4000	800	16
<input type="checkbox"/> 74 to 82	4000	900	18
<input type="checkbox"/> > 82	4000	1000	20

Heparin infusion adjustment

- Measure PTT 6 hours after initial bolus then adjust heparin per chart below **for 24 hours**
- **After 24 hours, use standard Heparin Protocol for 48 hours**

Patients Weight (kg)	Dose change	PTT < 36 sec	PTT 36-45 sec	PTT 46-60 sec	PTT 61 sec or greater
<input type="checkbox"/> 26 – 35	Bolus	2400 units	1200 units	1200 units	Therapeutic – No dose change
	Rate	↑ 2 mL/hour	↑ 2 mL/hour	↑ 1 mL/hour	
<input type="checkbox"/> 36 - 45	Bolus	3200 units	1600 units	1600 units	
	Rate	↑ 3 mL/hour	↑ 3 mL/hour	↑ 1 mL/hour	
<input type="checkbox"/> 46 – 55	Bolus	4000 units	2000 units	2000 units	
	Rate	↑ 4 mL/hour	↑ 3 mL/hour	↑ 2 mL/hour	
<input type="checkbox"/> 56 – 65	Bolus	4800 units	2400 units	2400 units	
	Rate	↑ 5 mL/hour	↑ 4 mL/hour	↑ 2 mL/hour	
<input type="checkbox"/> 66 – 75	Bolus	5600 units	2800 units	2800 units	
	Rate	↑ 6 mL/hour	↑ 4 mL/hour	↑ 3 mL/hour	
<input type="checkbox"/> 76 – 85	Bolus	6400 units	3200 units	3200 units	
	Rate	↑ 6 mL/hour	↑ 5 mL/hour	↑ 3 mL/hour	
<input type="checkbox"/> 86 – 95	Bolus	7200 units	3600 units	3600 units	
	Rate	↑ 7 mL/hour	↑ 5 mL/hour	↑ 4 mL/hour	
<input type="checkbox"/> 96 – 105	Bolus	8000 units	4000 units	4000 units	
	Rate	↑ 8 mL/hour	↑ 6 mL/hour	↑ 4 mL/hour	
<input type="checkbox"/> 106 – 115	Bolus	8800 units	4400 units	4000 units	
	Rate	↑ 9 mL/hour	↑ 6 mL/hour	↑ 5 mL/hour	
NEXT PTT DUE		IN 6-8 HRS	IN 6-8 HRS	IN 6-8 HRS	NEXT A.M.

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ADDITIONAL INFORMATION FOR PRESCRIBERS AND NURSES**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 perivascular 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)

THROMBOLYTIC THERAPY

ABSOLUTE CONTRAINDICATIONS (Do not use if any of the following are present)	RELATIVE CONTRAINDICATIONS
<ul style="list-style-type: none"> • 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) 	<ul style="list-style-type: none"> • 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

Alteplase preparation and administration instructions

1. Using a blunt 18 gauge needle, add 50 mL sterile water (provided by the manufacturer) to each 50 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. Withdraw alteplase 15 mg (15 mL) bolus into a syringe
3. Administer alteplase bolus dose over 2 minutes intraVENOUS push then immediately start alteplase infusion
4. Transfer remainder of both vials to an empty 150 mL sterile viaflex bag (supplied by pharmacy) and hang using standard IV tubing with no ports.
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. **Program STEP 1 INITIAL INFUSION dose over 30 minutes**
7. Upon completion of initial 30 minute infusion, program **STEP 2 SUBSEQUENT INFUSION over 60 minutes**
8. At 90 minutes/completion of infusion, stop the alteplase infusion and disconnect from IV Y site. Do not infuse any drug remaining in the tubing