Heparin-Induced Thrombocytopenia (HIT) Protocol

Purpose:

- To provide guidelines for the assessment of suspected HIT and its treatment with Argatroban
- Thrombosis prophylaxis in patients with history of HIT and contraindications for first-line therapies

Pre-Administration Criteria:

Definition: HIT is an adverse drug reaction characterized by thrombocytopenia and a high risk for venous or arterial thrombosis. It is caused by heparin-dependent, platelet-activating antibodies that recognize a "self" protein, platelet factor 4 (PF4), bound to heparin. The resulting platelet activation is associated with increased thrombin generation.

Consider HIT if:

- History of HIT or allergy to heparin
- Evidence of heparin or LMWH exposure within the last 100 days
- Thrombocytopenia (Platelets < 100,000/µL or >50% decrease from baseline)
- Clinical presentation of HIT with Thrombotic Syndrome (HITTS) i.e. DVT or PE

Suspected or Confirmed HIT:

- Discontinue ALL heparin products: IV, subcutaneous, flushes, heparin-coated catheters
- Place **NO HEPARIN** sign on door to patient's room and on all IV lines
- Document allergy to heparin in medical record with reaction noted as "severe" and reaction type "HIT"
- Notify pharmacist that patient has suspected HIT
- Consider hematologist consult

Baseline Labs:

- CBC, aPTT and PT/INR
- Heparin-PF4 Antibody ELISA (please note this is a *send-out laboratory test)*
- Liver Function Tests if not done during the previous 24 hours

Argatroban Precautions:

- Elevation of PT/INR during Argatroban therapy is due to the synergistic effect of Argatroban and warfarin and does not represent the patient's true coagulation status. DO NOT GIVE PLATELETS OR VITAMIN K.
- There are NO antidotes or reversal agents for Argatroban.
- Caution should be used in patients with severe hepatic impairment (LFTs > 3x normal).
- Use with caution if patient has a history of stroke, bleeding ulcers, severe uncontrolled hypertension, recent major surgery or non-compressible large vessel puncture.

Adult Argatroban Drip Protocol for HIT

Initiating Therapy:

- Only to be administered in ICU
- If patient was on heparin infusion, wait 3 hours prior to initiating Argatroban after discontinuation of heparin infusion. If patient is on LMWH, wait 8 hours prior to initiating Argatroban except in the case that the patient has an active clot while on these medications.
- If on warfarin at time of initiation: Reverse the warfarin using Vitamin K 5 mg PO x 1 AFTER Argatroban has started.
- Discontinue warfarin and fondaparinux.
- Discontinue aspirin doses greater than 162 mg/day
- Verify patient's total body weight in kilograms.
- Start a dedicated IV line for Argatroban infusion.
- Discontinue all IM or intrathecal injections.

Baseline aPTT: _____ seconds

Target aPTT: 55 – 100 seconds (1.5 to 3 times baseline, not to exceed 100 seconds)

Monitoring and Other Labs:

- Infuse using an IV pump
- Repeat aPTT after start of infusion:
    - Normal liver function: every 2 hours
    - Hepatic impairment or critically ill: every 4 hours
- Check aPTT daily once in target range for 2 consecutive checks
- Resume aPTT checks after each dosage adjustment:
    - Normal liver function: every 2 hours until in range for 2 consecutive checks
    - Hepatic impairment or critically ill: every 4 hours until in range for 2 consecutive checks
- CBC daily while on Argatroban
- Assess patient for signs of bleeding and notify physician immediately for:
    - Unexplained drop in blood pressure
    - Development of hematoma or gross bleeding
    - Recheck aPTT in 4 hours

Please see page 3 of this protocol for Argatroban dosing and titration.

Conversion to oral warfarin therapy:

- Once platelets are 150,000/µL or greater, initiate warfarin at a dose of no more than 5 mg.
- Continue concurrent Argatroban + warfarin combination therapy for at least 5 days and until the INR is within target range
- Measure daily INR when warfarin initiated
    - If INR less than 4, continue concomitant therapy and consider increasing warfarin dose
    - If INR greater than 4, stop Argatroban infusion and repeat INR in 4 hours
        - If INR is within range (INR = 2-3, unless otherwise specified), continue warfarin monotherapy
        - If INR is below range, resume Argatroban + warfarin combination therapy. Repeat process with next INR.

Argatroban standard concentration 250 mg/250 mL (1 mg/mL)

Initial infusion calculation (physician to select one)

- o Standard
- o Hepatic impairment (LFTs 3 x upper limit of normal)
- o Critically Ill + Multi-organ failure

Patient Weight (kg)	Standard (normal liver function)	Hepatic Impairment	Critically Ill + Multi-organ Failure
	2 mcg/kg/minute	0.5 mcg/kg/minute	0.2 mcg/kg/minute
INITIAL INFUSION RATE			
50-55 kg	6 mL/hr	1.5 mL/hr	0.6 mL/hr
56-60 kg	7 mL/hr	2 mL/hr	0.7 mL/hr
61-65 kg	7 mL/hr	2 mL/hr	0.7 mL/hr
66-70 kg	8 mL/hr	2 mL/hr	0.8 mL/hr
71-75 kg	9 mL/hr	2 mL/hr	0.9 mL/hr
76-80 kg	9 mL/hr	2 mL/hr	0.9 mL/hr
81-85 kg	10 mL/hr	2.5 mL/hr	1 mL/hr
86-90 kg	10 mL/hr	3 mL/hr	1 mL/hr
91-95 kg	11 mL/hr	3 mL/hr	1.1 mL/hr
96-100 kg	12 mL/hr	3 mL/hr	1.2 mL/hr
101-105 kg	12 mL/hr	3 mL/hr	1.2 mL/hr
106-110 kg	13 mL/hr	3 mL/hr	1.3 mL/hr
111-115 kg	13 mL/hr	3 mL/hr	1.3 mL/hr
116-120 kg	14 mL/hr	3.5 mL/hr	1.4 mL/hr
121-125 kg	15 mL/hr	4 mL/hr	1.5 mL/hr
126-130 kg	15 mL/hr	4 mL/hr	1.5 mL/hr
131-135 kg	16 mL/hr	4 mL/hr	1.6 mL/hr
136-140 kg	16 mL/hr	4 mL/hr	1.6 mL/hr
141-145 kg	17 mL/hr	4 mL/hr	1.7 mL/hr
146-150 kg	18 mL/hr	4 mL/hr	1.8 mL/hr
151-155 kg	18 mL/hr	4.5 mL/hr	1.8 mL/hr
156-160 kg	19 mL/hr	5 mL/hr	1.9 mL/hr
161-165 kg	19 mL/hr	5 mL/hr	1.9 mL/hr
166-170 kg	20 mL/hr	5 mL/hr	2 mL/hr
171-175 kg	21 mL/hr	5 mL/hr	2.1 mL/hr
176-180 kg	21 mL/hr	5 mL/hr	2.1 mL/hr
181-185 kg	22 mL/hr	5 mL/hr	2.2 mL/hr
186-190 kg	22 mL/hr	5.5 mL/hr	2.2 mL/hr
191-195 kg	23 mL/hr	6 mL/hr	2.3 mL/hr
196-200 kg	23 mL/hr	6 mL/hr	2.3 mL/hr

See page 4 of this protocol for titration instructions.

Argatroban continuous infusion titration:

1. Maximum rate of infusion is 10 mcg/kg/minute
   (To calculate max rate in mL/hr, take patient's weight in kg and multiply by 0.6).

2. Adjust infusion rate based on aPTT values as shown in the following table. Two nurses to perform independent calculations and co-sign rate changes.

aPTT	Rate Adjustment	Recheck aPTT from time of dose change	
		Standard (normal liver function)	Hepatic Impairment/ Critically Ill + Multi-organ Failure
≤ 34	↑ rate by 50% (multiply current rate by 1.5)	2 hours	4 hours
35-54	↑ rate by 25% (multiply current rate by 1.25)	2 hours	4 hours
GOAL 55-100	**NO CHANGE**	Continue every 2 hours until therapeutic x 2, then recheck every AM	Continue every 4 hours until therapeutic x 2, then recheck every AM
101-110	↓ rate by 25% (multiply current rate by 0.75)	2 hours	4 hours
111-120	↓ rate by 50% (multiply current rate by 0.5)	2 hours	4 hours
≥ 121	**Stop infusion**. Notify MD. STAT aPTT every 2 hours until between 55 and 100. Restart at 50% of previous rate (multiply rate by 0.5)	2 hours	4 hours

Conversion of Argatroban back to heparin:
If the patient is determined NOT to have HIT, may convert back to heparin infusion WITHOUT BOLUS, 2 hours after discontinuing Argatroban in consultation with attending physician. Notify pharmacy to have allergy removed from profile.

SPF-650-13