Adult Argatroban Drip Protocol

This protocol reflects current evidence based clinical practice.
It is not a substitute for appropriate clinical evaluation and does not supersede clinical judgment.

Exclusion Criteria:

1. Argatroban is not for use in patients with moderate to severe hepatic insufficiency.
2. No anticoagulation within 24 hours of therapeutic alteplase (tPA) for ischemic stroke.
3. No concurrent epidural analgesia, spinal, or lumbar puncture while anticoagulated.
4. If patient's PTT is greater than 100 or INR greater than 2.5 do NOT start Argatroban and notify attending physician.

Initiating Argatroban Therapy:

1. Only to be administered in ICU or DOU per Adult IV Administration Guidelines (Policy 100.025).
2. Use approved Adult Argatroban Drip PowerPlan: PHA Adult Argatroban Infusion Initiation (VCMC 345-040)
3. Obtain a Heparin Induced Thrombocytopenia (HIT) antibody with reflex Serotonin Release Assay to confirm HIT diagnosis. Argatroban infusion may be started before HIT antibody results are available.
4. Obtain baseline labs: PT, PTT, CBC and CMP.
5. Discontinue all heparin products: heparin infusion, subcutaneous heparin, enoxaparin (LMWH; Lovenox) and heparin flushes.
6. Discontinue warfarin and fondaparinux.
7. Discontinue aspirin doses that are greater than 162mg daily.
8. Discontinue all IM injections
9. Initiate argatroban within 2 hours after discontinuation of heparin infusion. For patients who were on therapeutic enoxaparin doses, initiate argatroban when next enoxaparin dose is expected to be given except in the case that the patient has an active clot. Obtain hematology consult to consider earlier initiation or argatroban. If patient was on prophylaxis dose of enoxaparin or heparin, start argatroban as clinically needed irrespective of time of previous enoxaparin/heparin dose.
10. **IF ON warfarin AT TIME OF INITIATION:** Reverse the warfarin using Vitamin K 5 mg PO X1 after argatroban has started; call Attending if patient is unable to take oral medications.
11. For patients with an acute MI or ACS obtain Hematology and Cardiology Consults.
12. Verify patient's total body weight in kilograms.
13. Start a dedicated IV line for argatroban infusion.

Dosing:

1. Standard argatroban infusion is 250 mg in 0.9% sodium chloride 250 mL, yielding a concentration of 1 mg/mL or 1,000 mcg/mL.
2. Therapeutic goal range for PTT is 55-100 seconds.
3. Initial infusion rate:
   a. 0.5 mcg/kg/min for patients with CHF, mild hepatic insufficiency, and critical illness.
   b. 1.2 mcg/kg/min for non-hepatically compromised patients.
4. Maximum rate of infusion is 10 mcg/kg/min
5. Adjust infusion rate based on PTT values as shown in the following table.. Two RNs must perform an independent double check. All rate changes including when rate is zero (0) must be documented on the MAR.

PTT	Rate Adjustment	Recheck PTT from time of dose change	
		Normal Hepatic Function	Impaired Hepatic Function /Critically Ill
≤ 34	↑ rate by 50% (**multiply rate by 1.5**)	2 hours	4 hours
35-54	↑ rate by 25% (**multiply rate by 1.25**)	2 hours	4 hours
GOAL 55-100	**NONE**	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	↓ by 25% (**multiply rate by 0.75**)	2 hours	4 hours
111-120	↓ rate by 50% (**multiply rate by 0.5**)	2 hours	4 hours
≥121	Stop infusion. Notify MD. Stat PTT every 2 hours until between 55 and 100. Restart at 50% of previous rate (**multiply rate by 0.5**)	2 hours	4 hours
For example, the rate is 0.5 mcg/kg/min and the first PTT = 33. The new rate is 0.75 mcg/kg/min (0.5 x 1.5).			

Monitoring:

1. Obtain PTT at 2 hours after initiation and after the time of all dose changes in patients with normal hepatic function; in patients with impaired hepatic function and critically ill patients, obtain PTT at 4 hours after initiation and after the time of all dose changes.
2. Repeat PTT every 2 hours (4 hours for patients with impaired hepatic function or critically ill) until therapeutic x 2.
3. Obtain a liver panel every 3 days or more frequently if indicated.
4. Obtain PT, PTT, and CBC daily.
5. **Call physician immediately for any of the following:** unexplained drop in blood pressure, unexplained tachycardia, the development of hematoma, drop in hemoglobin of >1g/dl, any signs of bleeding or gross hematuria.

Conversion to Oral Anticoagulation and Discontinuation of Argatroban:

See accompanying flow chart to determine timing of initiation of warfarin therapy and discontinuation of the argatroban infusion.

Conversion of Argatroban back to Heparin: *The use of heparin assumes the patient does not have heparin allergy or heparin-induced thrombocytopenia.

- If no hepatic insufficiency, start heparin infusion within 2 hours of stopping argatroban. Do not give loading dose.
- If there is hepatic insufficiency, start parenteral anticoagulant after 2-4 hours of stopping argatroban. Do not give loading dose.

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Argatroban Conversion to Warfarin Flow Chart

Co-administration of Warfarin plus Argatroban Infusion produces a synergistic increase in the INR that is usually NOT associated with increased bleeding risk. Expect co-therapy to continue for a minimum of 5 days.

Is the platelet count > 150,000?

- Yes → Initiate Warfarin at no more than 5mg PO daily
- No → Do NOT start Warfarin
  Continue Argatroban infusion
  Check Daily CBC, PT (INR), PTT

Initiate Warfarin at no more than 5mg PO daily

Co-administer Warfarin with Argatroban infusion for >120 hours regardless of INR

After 120 hours of Argatroban infusion + Warfarin co-administration
(Goal INR ≥ 4 during co-administration)

Patient WITH ACTIVE CLOT

	Argatroban dose > 2 mcg/kg/min	Argatroban dose ≤ 2 mcg/kg/min
INR < 4	1. Consider increase in the Warfarin dose while Argatroban remains therapeutic 2. Obtain hematology consultation regarding Warfarin and Argatroban management	
INR ≥ 4	1. Reduce Argatroban dose to 2 mcg/kg/min at 8am 2. At noon, obtain STAT PT (INR), PTT 3. Increase Argatroban back to prior dose without waiting for result of blood test 4. If PTT still therapeutic, lower Argatroban dose back down to 2mcg/kg/min and keep it there; go to column to right, A-E the next morning 5. If PTT subtherapeutic, obtain hematology consultation regarding Warfarin and Argatroban management	A. Hold Argatroban at 8am B. At 11am, draw STAT PT (INR) with Argatroban being held; only resume Argatroban if INR is subtherapeutic C. At 2pm, draw STAT PT (INR), then restart Argatroban at the previous rate after blood has been drawn; do NOT wait for result of INR D. May stop Argatroban when INR in therapeutic range (2-3 or 2.5-3.5) at the 11am and 2pm checks E. If INR not in therapeutic range, increase Warfarin per Warfarin guidelines and repeat steps A-D above

Patient withOUT clot

	Argatroban dose > 2 mcg/kg/min	Argatroban dose ≤ 2 mcg/kg/min
INR < 4	1. Consider increase in the Warfarin dose while Argatroban remains therapeutic 2. Obtain hematology consultation regarding Warfarin management	
INR ≥ 4	1. Reduce Argatroban dose to 2 mcg/kg/min regardless of PTT 2. Follow instructions in the column to the right, A-D starting that same day	A. Hold Argatroban at 8am B. At 2pm, draw STAT PT (INR) C. Restart Argatroban at the previous rate after blood has been drawn; do NOT wait for result of INR D. May stop Argatroban when INR in therapeutic range (2-3 or 2.5-3.5) at the 2pm check