

University of Maryland Medical Center

Argatroban (Argatroban®)

Continuous Intravenous Infusion Guidelines

BACKGROUND

- Argatroban is alternative anticoagulant in patients diagnosed with heparin induced thrombocytopenia (HIT), and **requires approval by Hematology prior to use**
- It is primarily metabolized by the liver and requires dose adjustments in patients with hepatic insufficiency. For patients with severe hepatic failure, consider alternative DTI.
- Half-life is 30 – 51 minutes for patients with normal hepatic function, 181 minutes for patients with hepatic impairment. Half-life is also prolonged in critically ill patients.

INITIATING ARGATROBAN INFUSION

1. Obtain patient weight, round down to nearest kilogram (kg)
2. Discontinue all active orders for heparin or low molecular weight heparin, including flushes or locks, and heparin in TPN
3. Discontinue all heparin coated catheters
4. Document heparin allergy (heparin induced thrombocytopenia) in chart
5. Draw baseline aPTT and PT/INR prior to infusion
6. Obtain baseline liver function tests
7. Begin argatroban infusion based on patient status or organ function:
 - a. For **non-critically-ill** patients with **normal hepatic function**:
Initiate argatroban infusion at **1 to 2 mcg/kg/min**
(Consider using lower rate for obese patients)
 - b. For **non-critically-ill** patients with **hepatic insufficiency**:
Initiate argatroban infusion at **0.5 mcg/kg/min**
 - c. For **critically ill** patients, patients with **reduced cardiac output**, OR **pediatric** patients:
Initiate argatroban infusion at **0.2 mcg/kg/min**

MONITORING AND ADJUSTING OF ARGATROBAN INFUSION

1. Adjust rate of argatroban infusion based on the following nomogram:
Note: Maximum infusion rate of argatroban is 10 mcg/kg/min
2. Goal aPTT is 46-75 seconds.
3. Check aPTT 2 hours after initiation of infusion and after any rate change
4. Adjust argatroban until aPTT is therapeutic, not exceeding aPTT greater than 100 seconds
5. When aPTT is within therapeutic range for 2 or more consecutive measures, check aPTT every 12 hours for 24 hours. If aPTT remains stable, check aPTT daily.
6. Monitor CBC, Hgb/Hct, signs/symptoms of bleeding daily

aPTT (sec)	Hold Infusion (min)	Critically Ill Patients OR Reduced Cardiac Function OR Pediatrics	Patients with Normal Hepatic Function	Next aPTT
< 45	0	Increase by 0.1 mcg/kg/min	Increase by 0.5 mcg/kg/min	2 hours after rate change
45 – 75	0	No Change	No Change	4 hours from last aPTT, if aPTT in range for 2 consecutive measures, check q12h
76 – 100	30	Decrease by 0.1 mcg/kg/min	Decrease by 0.5 mcg/kg/min	2 hours after rate change
> 100	Stop infusion	Check aPPT every 4 hours until aPPT <90. Restart infusion at 50% of previous rate		

CONVERSION TO ORAL ANTICOAGULATION FOR PATIENTS WITH HIT

1. Initiate warfarin **ONLY** after substantial platelet recovery, preferentially to normal (platelet $>100-150$ K/mm³).
2. Initiate warfarin dose at the expected maintenance dose. Loading dose should **NOT** be used. Avoid initial warfarin dose greater than 5 mg.
3. Overlap warfarin with argatroban for minimum of 5 days, and until INR is greater than 4. (INR goal = 4-6)
NOTE: argatroban can significantly increase the INR
4. At the end of overlap, if argatroban rate is less than 2 mcg/kg/min, stop infusion:
 - a. Obtain INR 4 to 6 hours after discontinuation of argatroban infusion
 - b. If INR is 2 to 3, continue with warfarin monotherapy
 - c. If INR is less than 2 (sub-therapeutic), resume argatroban at previous rate and repeat procedure the following day
5. At the end of the overlap, if argatroban rate is greater than 2 mcg/kg/min
 - a. Reduce infusion to 2 mcg/kg/min
 - b. Obtain INR 4 to 6 hours after the dose reduction
 - c. If INR is greater than 4, stop infusion and follow steps outlined in #4
 - d. If INR is less than 4, continue infusion and recheck INR the following day
6. Monitor for new thrombosis and limb ischemia while on warfarin therapy

References

1. Argatroban package insert. GlaxoSmithKline. 2009.
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3. Beiderlinden M, Treschan TA, Görlinger K, Peters J. Argatroban anticoagulation in critically ill patients. *Ann Pharmacother*. 2007;41:749-54.
4. Saugel B, Phillip V, Moessmer G, Schmid RM, Huber W. Argatroban therapy for heparin-induced thrombocytopenia in ICU patients with multiple organ dysfunction syndrome: a retrospective study. *Crit Care*. 2010;14(3):R90.
5. Levine RL, Hursting MJ, McCollum D. Argatroban therapy in heparin-induced thrombocytopenia with hepatic dysfunction. *Chest*. 2006;129:1167-1175.
6. Ansara AJ, Arif S, Warhurst RD. Weight-based argatroban dosing nomogram for treatment of heparin-induced thrombocytopenia. *Ann Pharmacother*. 2009;43:9-18.