Our Lady of the Lake Regional Medical Center
Pharmacy Anticoagulation Stewardship

Argatroban Infusion Protocol for Heparin Induced Thrombocytopenia (HIT) for Adult Patients

Indication: Treatment of heparin-induced thrombocytopenia with thrombosis syndrome (HITS) or thrombosis prophylaxis in patients with history of HIT and contraindications for first line therapies

Precautions:

1. Discontinue all sources of heparin (IV, SC, heparin flushes) and Low Molecular Weight Heparins
2. List 'Heparin Allergy' on patient's profile
3. Can cause false elevations of INR
4. Discontinue all IM injections
5. No concurrent epidural analgesia, spinal or lumbar puncture
6. No anticoagulant within 24 hours of tPA for ischemic stroke
7. Do not start Argatroban if PTT above 90 or INR above 2.5 – notify the physician

Initial labs:

- ☐ Baseline PT and aPTT and daily aPTT
- ☐ Baseline and daily CBC,
- ☐ Baseline CMP including LFTs
- ☐ aPTT 2 hours after starting Argatroban infusion and 2 hours after any rate change

Patient Care Orders:

- ☐ Check aPTT 2 hours after the start of infusion and 2 hours after any rate change
- ☐ Once 2 consecutive aPTT readings are within therapeutic range, check daily aPTT
- ☐ Notify the physician for any unexplained drop in blood pressure, unexplained tachycardia, greater than 1 g/dl drop in hemoglobin, gross hematuria or any overt signs of bleeding

Standard Argatroaban Infusion concentration: 1 mg/ml (250 mg / 250 ml
***** Maximum rate not to exceed 10 mcg/kg/min *****

- Use actual body weight up to 140 kg
- Maximum infusion rate 10 mcg/kg/min

Initial Infusion:

- **Non-ICU and ICU patients with no organ dysfunction:** **1 mcg/kg/min** Dose adjustment

aPTT (seconds)	Rate of Infusion	Check aPTT in hours
Below 35	Increase by 0.5 mcg/kg/min	2 hours
35 to 54	Increase by 0.25 mcg/kg/min	2 hours
55 to 100	NO change – continue current rate	When 2 consecutive readings within therapeutic range, start daily aPTT
101 to 110	Decrease by 0.25 mcg/kg/min	2 hours
111 to 120	Hold infusion for 1 hour and decrease by 0.5 mcg/kg/min	2 hours
Above 120	Stop infusion and call the physician	STAT PTT and check PTT q 2 hours

- **Patients with multi-organ dysfunction without concomitant hepatic and renal failure:** **0.5 mcg/kg/min** Dose adjustment

aPTT (seconds)	Rate of Infusion	Check aPTT in hours
Below 35	Increase by 0.25 mcg/kg/min	2 hours
35 to 54	Increase by 0.125 mcg/kg/min	2 hours
55 to 100	NO change – continue current rate	When 2 consecutive readings within therapeutic range, start daily aPTT
101 to 110	Decrease by 0.125 mcg/kg/min	2 hours
111 to 120	Hold infusion for 1 hour and decrease by 0.25 mcg/kg/min	2 hours
Above 120	Stop infusion and call the physician	STAT PTT and check PTT q 2 hours

- **ICU patient with moderate to severe hepatic dysfunction or combined hepatic/renal dysfunction:** **0.2 mcg/kg/min** Dose adjustment

aPTT (seconds)	Rate of Infusion	Check aPTT in hours
Below 35	Increase by 0.1 mcg/kg/min	2 hours
35 to 54	Increase by 0.05 mcg/kg/min	2 hours
55 to 100	NO change – continue current rate	When 2 consecutive readings within therapeutic range, start daily aPTT
101 to 110	Decrease by 0.05 mcg/kg/min	2 hours
111 to 120	Hold infusion for 1 hour and decrease by 0.1 mcg/kg/min	2 hours
Above 120	Stop infusion and call the physician	STAT PTT and check PTT q 2 hours

Transition to Warfarin[1]:

Consult clinical pharmacy,

a. Initiate warfarin after platelet count recovery.
    a. Platelet count is ≥ 150000/µl **OR**
    b. Platelet count is close to baseline for patient with previous chronic low platelet count.
b. Due to combined effect on INR when Argatroban is used concurrently with Warfarin. Loading doses of warfarin should **NOT** be used.

- Start Warfarin at a maximum dose of 5 mg daily, concurrently with argatroban infusion
- Obtain INR and follow the instructions below to determine when to stop argatroban infusion based on INR levels.

Patients receiving Argatroban at less than or equal to 2 mcg/kg/min:

Argatroban therapy can be stopped when combined INR on warfarin and Argatroban is above 4. Repeat INR in 4 to 6 hours. If INR below the desired therapeutic range, Argatroban infusion can be restarted. Repeat the procedure daily until INR on warfarin alone is within desired therapeutic range.

Patients receiving Argatroban at greater than 2 mcg/kg/min:

In order to predict the INR on Warfarin alone, reduce argatroabn dose to less than 2 mcg/kg/min and repeat the INR 4 to 6 hours after dose reduction. Argatroban infusion can be stopped when combined INR on Warfarin and Argatroabn is above 4. Repeat INR in 4 to 6 hours. If INR is below the desired therapeutic range, Argatroban infusion can be restarted. Repeat the procedure daily until INR on warfarin alone is within desired therapeutic range.

References:

1. Cuker, Adam, et al. American Society of Hematology 2018 Guidelines for Management of Venous Thromboembolism: Heparin-Induced Thrombocytopenia. American Society of Hematology. 2018; 2(22): 2260-3392.
2. Baroletti, S., Goldhaber, S.. Heparin-Induced Thrombocytopenia. American Heart Association. 2006; 114: e355-e356.
3. **Argatroban:** drug information **Lexicomp 22nd edition**
4. Argatroban Dosage requirements and Outcomes in Intensive Care versus Non-intensive Care patients **Pharmacotherapy, 2009; 29(9): 1073-1081**
5. A direct thrombin inhibitor argatroban: a review of its use in patients with and without HIT **Biologics; 2007, June 1(2): 105-112**
6. Argatroban Anticoagulation in Critically Ill Patients **Ann. Pharmacotherapy; 2007, 41(5):749-54**