**Purpose**

To provide caregivers at Cleveland Clinic Abu Dhabi (CCAD) with a standard protocol for using argatroban to treat patients with heparin induced thrombocytopenia (HIT).

**Protocol**

1. Ordering
   1. The physician would place an order to initiate argatroban specifying the initial infusion rate. If a baseline activated partial thromboplastin time (aPTT) is not available for the patient, the physician would place an order prior initiation of the infusion.
   2. Nursing would order the subsequent doses and aPTT as per protocol unless otherwise indicated per treating physician.
   3. A pharmacotherapy consult can be provided to help in the anticoagulation management and the transition to warfarin therapy.
2. Dosing protocol
   1. Goal aPTT: 45-70 sec, unless otherwise specified by the treating physician.
   2. For patients with prolonged baseline aPTT, contact hematology or pharmacy for recommendations on goal range.
   3. Dosing is based on ACTUAL body weight.
   4. Initial rate depends on the patient specific factors:
      1. Patient with normal liver function: start at 1 mcg/kg/min
      2. Patient with moderate-severe liver dysfunction (Child-Pugh classes B and C): start at 0.5 mcg/kg/min
      3. Critically-ill patients: consider a lower initial rate of 0.2-0.5 mcg/kg/min.
   5. The first aPTT is obtained 2 hours after the initial infusion is started.
   6. Subsequent adjustments and aPTT testing are based on the table below.
   7. Once 2 consecutive PTTs are within therapeutic range, repeat aPTT every 12hours.
   8. Notify MD for aPTT > 100 or outside goal range for 2 consecutive measures.
3. Adjustment tables

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| **Table 1: Normal liver function and non-critically ill patients** | | |
| **aPTT** | **Dose/Rate (mcg/kg/min)** | **Next aPTT** |
| < 37 sec | Increase by 0.5 mcg/kg/min | 4hours |
| 37-45 sec | Increase by 0.25 mcg/kg/min | 4hours |
| 45-70 sec | No change | 4hours. After 2 consecutive aPTT within range, check aPTT every 12h |
| 71-99 sec | Decrease rate by 0.25 mcg/kg/min.  If current rate is < 0.5 mcg/kg/min, use 0.5 times the current rate | 4hours |
| ≥ 100 sec | Hold infusion for 2 hours; resume at 50% of the rate when aPTT <100 sec | Repeat every 2hours until aPTT <100 sec |

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| **Table 2: Hepatic dysfunction and/or critically ill patients** | | |
| aPTT | **Dose/Rate (mcg/kg/min)** | **Next aPTT** |
| < 37 sec | increase by 0.2 mcg/kg/min | 4hours |
| 37-45 sec | increase by 0.1 mcg/kg/min | 4hours |
| 45-70 sec | No change | 4hours. After 2 consecutive aPTT within range, check aPTT every 12h |
| 71-99 sec | Decrease rate by 0.1 mcg/kg/min.  If current rate is < 0.2 mcg/kg/min, use 0.5 times the current rate | 4hours |
| ≥ 100 sec | Hold infusion for 2 hours; resume at 50% of the rate when aPTT <100 sec | Repeat every 2hours until aPTT <100 sec |

1. Pharmacy will dispense argatroban in a concentration of 1mg/mL (250mg/250mL).
2. In patients diagnosed with heparin induced thrombocytopenia, warfarin will be started and continued for a minimum of 4 weeks (for HIT without thrombosis) or 3 months (for HIT with thrombosis).
3. The following needs to be taken into consideration while transitioning to warfarin therapy.
   1. Warfarin will be initiated once platelets recover to > 150,000.
   2. Argatroban falsely elevates international normalize ratio (INR): a laboratory interaction, not an increased anticoagulant effect.
   3. The overlap with Argatroban and Warfarin should continue for a MINIMUM of 5 days and until the INR is within the target range:
      1. **Patients receiving <2mcg/kg/min of argatroban**: stop argatroban when the combined INR on warfarin and argatroban is >4. Repeat INR measurement 4-6 hours later. If INR is below therapeutic level, resume argatroban therapy. Repeat procedure daily until desired INR on warfarin alone is obtained.
      2. **Patients receiving >2mcg/kg/min of argatroban**: reduce the dose of argatroban to 2mcg/kg/min; measure INR for argatroban and warfarin 4-6 hours after dose reduction; argatroban therapy can be stopped when the combined INR on warfarin and argatroban is >4. Repeat INR in 4-6 hours; if INR is below the therapeutic level argatroban may be re-started. Repeat procedure daily until desired INR on warfarin alone is obtained.

**Oversight and Responsibility**

1. Department of Pharmacy Services
2. Department of Hematology Oncology

**Definitions**

1. None

**References**

1. Linkins LA, Dans AL, Moores LK. Treatment and prevention of heparin-induced thrombocytopenia: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012 Feb;141(2 Suppl):e495S-530S. doi: 10.1378/chest.11-2303.

**Institute / Department / Committee Involved in Protocol Development / Revision**

1. Pharmacotherapy
2. Respiratory and Critical Care Institute (RCCI)

**Contact for Questions / Clarifications**

1. Manager of Pharmacotherapy Services
2. Hematologist / Oncologist

**Related or Supporting Documents:**

1. None

**Abbreviation**

1. aPTT- Activated Partial Thromboplastin Time
2. CCAD- Cleveland Clinic Abu Dhabi
3. HIT- Heparin Induced Thrombocytopenia
4. INR- International Normalize Ratio
5. RCCI- Respiratory and Critical Care Institute