Before administering argatroban, discontinue heparin therapy and obtain a baseline aPTT. The recommended initial dose of argatroban is 0.5 mcg/kg administered via a large bore intravenous infusion. The dose for patients with or at risk for heparin-induced thrombocytopenia undergoing percutaneous coronary intervention (PCI) at a dose of 5 mcg/kg administered over a 60-second period is not recommended.

The area for patients with or at risk for heparin-induced thrombocytopenia undergoing percutaneous coronary intervention (PCI) at a dose of 5 mcg/kg administered over a 60-second period

- **Table 1. Recommended Starting and Maintenance Doses (Within the Target ACT Range) of Argatroban Injection in Patients Undergoing PCI**
  - **Initial Dosage:**
    - ACT range: 300-450 seconds
    - Initial dose: 0.5 mcg/kg administered via a large bore intravenous infusion
  - **Dosage Adjustment:**
    - Greater than 450 seconds: no bolus dose is given if ACT greater than 450 seconds

- **Monitoring Therapy:**
  - Tests of anticoagulant effects (including the aPTT) typically attain steady-state levels within 1 to 3 hours following initiation of argatroban therapy. For use in PCI, therapy with Argatroban Injection is monitored using ACT. Obtain ACTs before dosing, 5 to 10 minutes after bolus dosing, following initiation of the continuous infusion, at scheduled times, and as clinically indicated. In clinical trials in PCI, the activated clotting time (ACT) range was used as a therapeutic index.

- **Special Considerations:**
  - Patients may have experienced more than one adverse event.
  - Table 7 gives an overview of the most frequently observed non-hemorrhagic events (>2%), sorted by decreasing frequency of occurrence among patients who underwent PCI.

- **Adverse Reactions:**
  - Nausea, vomiting, nausea, vomiting, or taking time to account for the impact of the drug on the patient. Discontinue Argatroban Injection if the patient develops severe symptoms, such as severe nausea or vomiting.

- **Contraindications:**
  - Severe hypersensitivity to argatroban, ion exchange resin-based dialyzers, or any component of the product
  - Concomitant use of argatroban with antiplatelet agents, thrombolytics, and other anticoagulants may increase the risk of bleeding.

- **Warnings and Precautions:**
  - Cardiac arrest
  - Ventricular tachycardia
  - Cardiac arrest
  - Diarrhea
  - Fever
  - Bradycardia
  - Hypotension
  - Heparin-induced thrombocytopenia

- **Dosage and Administration:**
  - Infusion Rate: 100 mcg/kg/hour
  - Titrate to maintain ACT near the lower limit of the target range

- **Reconstitution:**
  - Reconstitute Argatroban Injection with Sterile Water for Injection and administer the reconstituted solution as an intravenous infusion over 1 hour or as a continuous infusion at a rate of 100 mcg/kg/hour.

- **Previous Administration:**
  - If the patient has received another anticoagulant, discontinue the previous anticoagulant and administer Argatroban Injection as soon as possible.

- **Re-exposure:**
  - If a patient has been re-exposed to argatroban, the therapeutic ranges for these tests have not been identified for argatroban therapy. In clinical trials in PCI, the activated clotting time (ACT) range was used as a therapeutic index.

- **Additional Information:**
  - Argatroban Injection is intended only for use with ACT monitors using flow-through technology. The ACT ranges based on a target ACT of 300-450 seconds are 350-450 seconds, 400-500 seconds, and 450-600 seconds for ACT monitors with flow-through technology and 250-350 seconds, 300-400 seconds, and 400-500 seconds for ACT monitors without flow-through technology.

- **Pharmacokinetics:**
  - The pharmacokinetics of argatroban are linear and dose-proportional. The steady-state aPTT is proportional to the argatroban dose.

- **Clinical Studies:**
  - A randomized, double-blind, placebo-controlled study of Argatroban Injection was conducted in patients undergoing PCI.

- **References:**
  - Argatroban Injection is contraindicated in patients with a history of disseminated intravascular coagulation (DIC) or who are at high risk of developing DIC. Argatroban Injection should be used with caution in patients with hepatic impairment.

- **Additional Information:**
  - Argatroban Injection is contraindicated in patients with a history of disseminated intravascular coagulation (DIC) or who are at high risk of developing DIC. Argatroban Injection should be used with caution in patients with hepatic impairment.
Argatroban is a specific, potent, direct thrombin inhibitor. It is indicated for the prevention and treatment of heparin-induced thrombocytopenia (HIT) and HIT--thrombosis syndrome (HITTS)
and is contraindicated in patients who have had an anaphylactic reaction to argatroban. Patients should be informed of the risks associated with Argatroban Injection as well as the plan for regular monitoring during administration of the drug. 

**Dosage and Administration (2.5)**

There were 22 serious adverse events in 17 PCI patients (19.6% in 112 interventions). Table 8 lists the serious adverse events occurring in these patients. The most common serious adverse events were gastrointestinal hemorrhage and allergic reactions. The incidence of gastrointestinal hemorrhage was 8.0% in the argatroban group and 2.8% in the control group. The incidence of allergic reactions was 2.8% in the argatroban group and 1.8% in the control group.

**Adverse Reactions (7.3)**

**Gastrointestinal hemorrhage**

- Severe: 2.5% in the argatroban group and 1.7% in the control group.
- Moderate: 5.0% in the argatroban group and 3.0% in the control group.
- Mild: 8.0% in the argatroban group and 2.8% in the control group.

**Allergic reactions**

- Severe: 2.8% in the argatroban group and 1.8% in the control group.
- Moderate: 2.8% in the argatroban group and 1.8% in the control group.
- Mild: 2.8% in the argatroban group and 1.8% in the control group.

**Interactions (7.2)**

**Heparin**

- The dose of heparin should be adjusted to achieve an aPTT level within the recommended range of 50 to 80 seconds. If the aPTT level is above 80 seconds, the dose of heparin should be decreased. If the aPTT level is below 50 seconds, the dose of heparin should be increased.

**Pharmacodynamics**

- Argatroban has a time-dependent inhibition of thrombin activity. The duration of inhibitory activity is dependent on the duration of drug exposure.

**Pharmacokinetics**

- The oral bioavailability of argatroban is approximately 20%.

**Metabolism**

- Argatroban undergoes hepatic metabolism, via CYP3A4/5-mediated metabolism, to form metabolites that are excreted in the urine.

**Excretion**

- About 65% of the dose of argatroban is excreted in the urine as metabolites, and about 20% is excreted in the bile.

**Precautions (7.1)**

**Hepatic impairment**

- The dosage of argatroban should be decreased in patients with hepatic impairment. The dosage should be reduced to 0.75 mcg/kg/min. The dosage should be increased in patients with severe hepatic impairment.

**Hypersensitivity**

- Argatroban has been associated with anaphylactic reactions. Patients should be monitored for signs of hypersensitivity during and after administration of the drug.

**Pregnancy (8.1)**

- Argatroban is classified as Pregnancy Category B. Studies in animals have shown no evidence of impaired fertility or harm to the fetus. Because animal reproductive studies are not always predictive of human response, this drug should be used during pregnancy only if the potential benefit justifies the potential risk.

**Lactation (8.3)**

- Argatroban may cause harm to the nursing infant. Infants of nursing mothers should be monitored for signs of harm. Patients should be informed that breastfeeding is not recommended during the administration of argatroban.