Bivalirudin

Brand names	Angiomax
Medication error potential	ISMP high-alert medication that has an increased risk of causing significant patient harm if it is used in error[1]
Contraindications and warnings	**Contraindications:** Active major bleeding, hypersensitivity to bivalirudin or any product component[2] **Warnings:** Hemorrhage can occur at any site. **Coronary artery brachytherapy:** Risk of thrombus formation, including fatal outcomes, in gamma brachytherapy[2]
Infusion-related cautions	None noted[2]
Dosage	The manufacturer states that the safety and efficacy in pediatric patients has not been established.[2] **Dosing adjustment for obesity:** A review of 135 *adults* with heparin-induced thrombocytopenia (HIT) concluded that doses should be based on total body weight.[3] **Percutaneous catheterization/intravascular procedures:** Limited duration infusions/targeting higher state of anticoagulation (e.g., activated clotting time [ACT] >300 seconds) Bolus 0.75 mg/kg followed by an infusion of 1.75 mg/kg/hr during procedure.[4,5] One case report describes lower dosing of 0.5 mg/kg bolus and 0.25 mg/kg/hr during procedure.[6] **Anticoagulation for thrombosis/HIT, extracorporeal membrane oxygenation (ECMO) or ventricular assist devices (VAD):** Longer duration infusions/targeting lower state of anticoagulation (e.g., ACT 160–200 seconds, or activated partial thromboplastin time [aPTT] 1.5–2.5 × baseline or approximately 50–90 seconds). Data from small studies or case reports. Follow institutional or device-specific protocols. **Thrombosis/HIT:** Data from two small studies, *n* = 16 each. Bolus dose (if desired) 0.125–0.5 mg/kg followed by initial infusion of 0.05–0.25 mg/kg/hr. Infusions of up to 0.55 mg/kg/hr have been required.[7,8] **ECMO:** Bolus (not uniformly used, especially if patient already anticoagulated with another agent) 0.04–0.14 mg/kg (*n* = 12 patients, 1 day–6 years old)[9] to 0.4 mg/kg (*n* = 1, neonate on ECMO with HIT).[10] Reported infusion doses range from 0.03–0.48 mg/kg/hr.[9-11] **VAD:** One study described a protocol for anticoagulation and antiplatelet therapy for the Berlin Heart EXCOR VAD in six patients (age 0.8–14 years).[12] No bolus. Initial infusion at 0.5 mg/kg/hr titrated to goal aPTT 1.5–2.5 × baseline or 60–90 seconds, or ACT 180–220 seconds. The median therapeutic bivalirudin dose was 0.7 mg/kg/hr (range, 0.1–0.8 mg/kg/hr). Refer to study for full protocol including antiplatelet therapy recommendations.
Dosage adjustment in organ dysfunction	**Renal dysfunction:** No reduction needed for bolus dose. In addition to monitoring the anticoagulation state of the patient, the manufacturer recommends the following infusion dose adjustments for *adults* undergoing percutaneous coronary interventions with target ACT generally >225 seconds[2]: **CrCl ≥30 mL/min:** 1.75 mg/kg/hr (i.e., no adjustment required) **CrCl <30 mL/min:** 1 mg/kg/hr **Hemodialysis:** 0.25 mg/kg/hr

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Dosage adjustment in organ dysfunction *(cont.)*	A pediatric study (protocol for VAD anticoagulation; goal aPTT 1.5–2.5 × baseline or 60–90 seconds; goal ACT 180–220 seconds) described the following infusion adjustments for renal dysfunction[12]: **GFR 30–60 mL/min:** 0.3 mg/kg/hr **GFR <30 mL/min:** 0.2 mg/kg/hr **Renal replacement therapy:** 0.1 mg/kg/hr **Plasma exchange:** A case report described successful maintenance of anticoagulation in an 8-year-old child on ECMO and undergoing plasma exchange. The bivalirudin infusion was increased by about 25% to 30% at the beginning of the exchange and reduced back to baseline or near baseline at the completion of the exchange. Bolus doses were also given (approximately 0.7–0.9 mg/kg each) during the exchange to maintain goal aPTT (60–80 seconds).[13]
Maximum dosage	Indication-specific. See the Dosage section. Titrate infusion to goal aPTT or ACT range.
Additives	Each 250-mg vial of bivalirudin contains 125 mg mannitol[2] and 12.5 mg sodium.[14]
Suitable diluents	Reconstitute with SWFI. Dilute further with D5W or NS.[2]
Maximum concentration	5 mg/mL[2]
Preparation and delivery	*Parenteral products should be visually inspected for particulate matter and discoloration before use. Refer to appropriate reference for more information on compatibility with other drugs and solutions, compatibility following Y-site delivery, and suggested storage and extended stability.*[14]
IV push	0.5–5 mg/mL[2]
Intermittent infusion	0.5–5 mg/mL.[2] One study reported using a concentration of 0.1 mg/mL as a sheath flush during percutaneous intravascular procedures.[4]
Continuous infusion	0.5–5 mg/mL[2]
Other routes of administration	IV administration only per manufacturer[2]
Comments	**Monitoring:** Coagulation status should be monitored. Manufacturer recommends ACT.[2] ACT results may vary depending on the type or assay characteristics of ACT test performed.[2,4] Many published studies report the use of multiple tests to analyze overall state of anticoagulation, especially for ECMO or VADs.[11,12] **Pharmacokinetic considerations:** Molecular weight 2180 daltons. Approximately 25% is cleared by hemodialysis.[2] **Pharmacodynamic considerations:** The anticoagulant effect is achieved immediately after IV administration, and coagulation tests return to baseline approximately 1 hour after cessation of infusion.[2] **Drug interactions:** Coadministration with heparin, warfarin, thrombolytics, or glycoprotein IIb/IIIa inhibitors was associated with an increased risk of major bleeding in clinical trials.[2]