GUIDELINES FOR THE USE OF LEPIRUDIN (REFLUDAN)

INDICATIONS:

Lepirudin is indicated for anticoagulation in patients with heparin induced thrombocytopenia (HIT) and associated thromboembolic disease in order to prevent further thromboembolic complications.

CONTRAINDICATIONS:

- Hypersensitivity to hirudins.

Dosage and Administration of Lepirudin

Lepirduin Dosing in "Normal" Renal Function (CrCl > 60 mL/min):

1. Bolus with 0.4 mg/kg (up to 110 kg) IV push over 1 minute. Max dose = 44 mg.
2. Follow bolus with continuous infusion at 0.15 mg/kg (up to 110 kg)/hour. Max infusion rate = 16.5 mg/hr.
3. Reduce both bolus and infusion rates as outlined below for renal insufficiency.
4. Obtain aPTT 4 hours after initial lepirudin bolus.
5. Follow adjustment nomogram for a target aPTT of 50-75 seconds.
6. Monitor platelet counts daily until recovery.

Lepirudin Dosing in Renal Insufficiency (CrCl < 60 mL/min):

1. Bolus with 0.2 mg/kg (up to 110 kg) IV push over 1 minute. Max dose = 22 mg.
2. Follow bolus with continuous infusion as below based upon creatinine clearance:

CrCl (mL/min)	S Cr	Dose (mg/kg/hr) {max = 8.25 mg/hr}
45-60	1.6-2.0	0.075 mg/kg/hr
30-44	2.1-3.0	0.045 mg/kg/hr
15-29	3.1-6.0	0.0225 mg/kg/hr
< 15	> 6.0	avoid or stop infusion

Evaluation & Management of a Patient if Heparin-Induced Thrombocytopenia (HIT) is Suspected

1. Distinguish between the two types of HIT:

	NI-HAT§	HIT¶
Frequency	10-20%	2-30%
Timing of onset	1-4 days	5-10 days
Nadir platelet count	100,000	30,000-55,000
Antibody mediated	No	Yes
Thromboembolic sequelae	None	30-80%
Hemorrhagic sequelae	None	Rarely

§NI-HAT = non-immune heparin associated thrombocytopenia (old term = HIT type 1)

¶ HIT = heparin-induced thrombocytopenia (old term = HIT type 2 or HITTS)

2. If NI-HAT:
   a. Continue heparin if clinically indicated
   b. Monitor daily platelet count until recovery

3. If HIT:
   a. Discontinue all sources of heparin (including heparin coated catheters, flushes, dialysate, etc.)
   b. Document the syndrome with a laboratory antibody assay
   c. Start lepirudin
   d. Avoid Coumadin for 5-7 days
   e. Monitor platelet counts daily until recovery
   f. Avoid prophylactic platelet transfusions.
   g. Antibodies are expected to disappear within 3 months.
   h. In general, patients with a history of HIT should be advised to avoid heparin exposure for life. One exception may be cardiac surgery.

Dosage Modifications

1. If aPTT is outside the therapeutic range, confirm this value with a repeat aPTT before a dose adjustment is made; unless clinical need to react immediately.
2. Adjustment Nomogram:

aPTT (sec)	Lepirudin dose/change
< 50	Increase infusion rate by 20%
50-75	**No Change**
> 75	Hold for 2 hrs, then decrease infusion by 50%

3. Obtain aPTT 4 hours after every change, then daily.

Management of a Patient if HIT is Suspected or Documented and Requires Cardiac Surgery

Elective Cardiac Surgery

1. Wait a minimum of 3 months.
2. Repeat laboratory assay for heparin antibodies.
3. If negative, proceed with surgery.
   a. Consider off-pump
   b. Some anecdotal reports exist supporting full heparinization during the procedure without postoperative administration.
   c. Consider use of lepirudin depending on severity of previous HIT episode.

Emergent Cardiac Surgery - Limited case report information

1. Consider off pump case.
2. Bolus dose of lepirudin of 0.2 mg/kg added to the prime and a 0.25 mg/kg IV bolus followed by a continuous infusion of 0.5 mg/min begun 5 minutes before cannulation for CPB.
3. Monitor ACT and/or aPTT every 10 minutes.
4. Administer 5-10 mg bolus as needed to maintain ACT > 350 sec and aPTT > 240 sec.

ã IHC 1999

Questions, Assistance, or Referrals:

LDSH: 408-1100 MCKAY-DEE: 398-2800 UTAH VALLEY: 357-7850 LifeFlight: 408-1234 or 1-800-408-1911