

**THEDACARE HOSPITALS
LEPIRUDIN (REFLUDAN) DOSING PROTOCOL**

Indication: Anticoagulation in patients with heparin-induced thrombocytopenia (HIT) – Immune mediated and associated thromboembolic disease.

Dosing and Administration: Prior to initiation, obtain a baseline aPTT, CBC, and serum creatinine, to determine creatinine clearance.

***** Normal Renal Function *****

If CrCl > 60 ml/min, then initial dosage is as follows:

Bolus: 0.4 mg/kg administered over 15-20 seconds IV push.

Initial Infusion: 0.15 mg/kg/hr as continuous infusion, start immediately after the bolus dose.

****** Adjustment for Renal Impairment******

If CrCl is ≤ 60 ml/min, then initial dosage is as follows:

Bolus: 0.2 mg/kg administered over 15-20 seconds IV push.

Initial infusion for Renal impairment. Start immediately after the bolus dose.

Creatinine clearance (ml/min)	% of standard initial infusion rate	Initial infusion mg/kg/hr
45-60	50 %	0.075
30-44	30 %	0.045
15-29	15 %	0.0225
Below 15 **	Avoid or STOP infusion	

**In hemodialysis patients or in cases of acute renal failure (CrCl<15 or SCr>6), infusion of lepirudin is to be avoided or stopped. Additional IV bolus doses of 0.1 mg/kg body weight should be considered every other day only if the aPTT ratio falls below the lower therapeutic limit of 1.5.

******General Dosing Notes******

* Actual body weight is used for calculating dose (up to 110 kg). If the patient weighs more than 110 kg, the initial dose should not be increased above the dose based on 110 kg (max initial bolus = 44 mg, max initial infusion = 16.5 mg/hr)

Monitoring

Patients with baseline aPTT ratio of 2.5 or greater, should not be started on lepirudin.

The infusion rate should be adjusted according to the aPTT ratio (the patient's aPTT at a given time over an aPTT reference range, usually median of the laboratory normal range for aPTT.)

The target range for the aPTT ratio is 1.5-2.5, which corresponds in our institution to an aPTT of **42-70 seconds**. (Studies have shown that aPTT ratios higher than this range did not reduce risk of thrombosis, while the risk for bleeding increased substantially.)

The first aPTT should be obtained 4 hours after the start of the infusion.

aPTT determinations should be obtained 4 hrs after a change in infusion rate or administration of an IV bolus.

Once the aPTT is in the target range for 2 consecutive checks, the aPTT should be checked daily.

More frequent aPTT monitoring is recommended in those with renal impairment, changing renal function, serious liver injury or with an increased risk of bleeding.

Dose Modifications

aPTT result	Adjustment	Recheck aPTT
< 28	Bolus 0.2 mg/kg, increase rate by 30%	4 hrs after rate change
28-41.9	Increase rate by 20 %	4 hrs after rate change
42-70	None	In 4hrs. After 2 consecutive measurements in this range, change to QAM checks.
70.1-84	Hold x 1 hr, decrease rate by 25 %	4 hrs. after restarting infusion
> 84	Hold x 2 hrs, decrease rate by 50 %	4 hrs. after restarting infusion

Important Notes

When HIT is suspected it is imperative that all forms of heparin are discontinued immediately, and that treatment with a direct thrombin inhibitor not be delayed while awaiting laboratory confirmation of HIT. The risk for a clinical event is highest when there is a delay in therapy. Enter a heparin allergy on the patient's profile and enter a pharmacy communication order indicating that the patient should not receive heparin or any heparin like products.

It is recommended to delay the start of warfarin until platelet counts are normalizing (>100,000-150,000) and clinical status has improved. Therapy with warfarin early on can result in venous limb gangrene due to the inhibition of protein C and S.

Warfarin should then be started at low doses (maximum 5 mg); therapy should overlap with lepirudin for at least 4-5 days and should not be discontinued until the INR is therapeutic for 2 consecutive days.

Concomitant treatment with thrombolytics may: Increase the risk of bleeding complications. Considerably enhance the effect of lepirudin on aPTT prolongation. If lepirudin is used concomitantly with thrombolytics, it is suggested to use a lower bolus and initial infusion rate of lepirudin.

Serious liver injury (eg, liver cirrhosis) may enhance the anticoagulant effect of lepirudin due to coagulation defects secondary to reduced generation of vitamin K-dependent clotting factors.

Lepirudin has no antidote. It binds irreversibly to 2 sites on thrombin.

REFERENCES: Available upon request