BIVALIRUDIN – the sole DTI on the UW Medicine Formulary as of November 2009

1. Why were argatroban and lepirudin removed from the UW Medicine Formulary?

In an effort to simplify care and contain costs, bivalirudin was selected as the single DTI for the formularly. Over 90% of DTI use at UWMC/HMC for the last several years has been with bivalirudin. It has the shortest elimination half-life of the three drugs, mixed clearance (renal and proteolyic cleavage) and is less expensive than argatroban.

2. How is bivalirudin dosed for patients with HIT who have in renal impairment?

Because of its partial renal clearance, the t1/2 of bivalirudin increases as Clcr declines, and dose adjustments are necessary (see below). The DTI assay (goal 60-90 seconds) should be used to guide dosing in all patients, including those with renal impairment, as individual patients with renal impairment may have different dosing requirements than anticipated by known pharmacokinetic parameters.

Clcr	T ½	Dose recommendation for HIT
> 60	25 min	0.15 mg/kg/hr
30-60	34 min	0.08 mg/kg/hr
< 30	57 min	0.05mg/kg/hr
Dialysis-dependent patients (off dialysis)	3-5 hrs	0.02 mg/kg/hr

3. How does dialysis impact bivalirudin?

Hemodialysis filters appear to clear about 25% of bivalirudin. Dosing requirements may be somewhat different off HD than on, and should be guided by DTI assay results.

Limited experience suggests that bivalirudin dosing requirements are similar in patients on CRRT, CVVH and CVVHDF, and may be somewhat higher than in patients on HD (0.03-0.04 mg/kg/hr). Nevertheless, UWMC guidelines suggest starting at a lower dose in these patients (0.02 mg/kg/hr), and adjusting upward if necessary based on DTI assay results.

4. Are there any references to turn to for more information on using bivalirudin in patients with renal impairment?

Kiser TH et al. Safety, efficacy and dosing requirements of bivalirudin in patients with heparin-induced thrombocytopenia. Pharmacotherapy 2008; 28:1115-24.

Kiser TH et al. Evaluation of bivalirudin treatment for heparin-induced thrombocytopenia in critically ill patients with heparin and/or renal dysfunction. Pharmacotherapy 2006; 26:452-60.

5. How dose obesity impact bivalirudin?

Bivalirudin dosing should be based on total body weight. The dose should not be capped above a certain limit. Patients up to 202 kg have been included in clinical trials, and there is no signal from clinical experience that higher body weight patients require any modification of dosing. Dosing adjustments should be made solely based on DTI assay results.

6. Where can I find the UWMC guidelines for the use of bivalirudin.

Current guidelines are located at www.uwmcacc.org, in the section on Heparin-Induced Thrombocytopenia. A bivalirudin order form is in development, and a nurse-managed protocol is being considered.