

## 20. PARECOXIB SODIUM, AN INJECTABLE COX-2 SPECIFIC INHIBITOR, DOES NOT AFFECT HEPARIN-REGULATED BLOOD COAGULATION PARAMETERS

Noveck, R.J.<sup>1</sup>; Kuss, M.E.<sup>2</sup>; Qian, J.<sup>2</sup>; North, J.<sup>2</sup>; Hubbard, R.C.<sup>2</sup> 1. Clinical Research Center, New Orleans, LA; 2. Pharmacia Corporation, Skokie, IL

**Introduction:** Parecoxib sodium is an injectable prodrug of the novel COX-2 specific inhibitor, valdecoxib. COX-2 specific inhibitors are effective in treating pain and inflammation without inducing side effects, such as inhibition of platelet function, observed with conventional NSAIDs. The objective of this study was to evaluate the effects of parecoxib and heparin, both alone and when coadministered, on blood coagulation parameters in healthy male subjects.

**Methods:** In treatment period I of this open-label pharmacodynamic interaction study, 23 healthy volunteers received a bolus injection of heparin (4000 U) immediately followed by a minimum 36-hour infusion, starting at a dose of 10-14 U/kg and adjusted to achieve a target activated partial thromboplastin time (aPTT) of 1.5-3.0x baseline value. Subjects with the most stable aPTT proceeded to treatment period II. After a 2-day washout, 18 subjects received intravenous parecoxib sodium 40 mg BID for 6 days. On day 5, subjects received a bolus (4000 U) injection of heparin followed by a 36-hour infusion at the same stable rate as determined during treatment period I. Prothrombin time (PT), aPTT, and platelet count were measured at baseline, during dosing, and at a posttreatment visit.

**Results:** Platelet counts and PTs before treatment and following heparin infusion alone (period I) were similar to those following the coadministration of parecoxib and heparin infusion (period II). Representative aPTT values in the 18 volunteers who completed both treatment periods of the study are shown in the table. Adverse events were of mild to moderate severity. Clinical laboratory values did not change from baseline throughout the study period.

**Conclusions:** Coadministration of parecoxib and heparin produced no clinically significant differences in platelet counts, PTs, or aPTTs when compared with heparin administration alone in healthy male volunteers. Intravenous administration of parecoxib and heparin were safe and well tolerated.

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APTT, seconds (mean±SD)		
Sampling Time	Heparin (Period I; n=23)	Heparin + Parecoxib (Period II, Days 5-7; n=18)
30 min before start of heparin (period I) or parecoxib (period II)	26.7±2.2	26.0±2.1*
6 h after start of heparin	74.5±40.0	79.2±32.0*
24 h after start of heparin	54.1±11.5	52.6±13.2*
36 h after start of heparin	50.9±14.8	47.7±8.6*
12-24 h after end of heparin	25.6±2.8	26.2±1.7*

\* $p > 0.05$  for all comparisons with heparin administration.