



THE **MEDICINES** COMPANY®

29th October 2007

Dear Healthcare Professional

IMPORTANT SAFETY INFORMATION

Angiox® (bivalirudin): use of inappropriate dosing regimens in European registry study

Further to discussions with the Irish Medicines Board, The Medicines Company UK Ltd. would like to draw your attention to the approved dosing regimen for Angiox®, which is approved in the EU for use in patients undergoing percutaneous coronary intervention (PCI). **The approved dose is a 0.75mg/kg bolus dose, followed by a 1.75mg/kg/hour infusion for the duration of the intervention.**

We have recently become aware of dosing practices that are not in accordance with the approved regimen in some European countries. Data from a recent registry study sponsored by the Nycomed Group (ImproveR) involving 4,000 European patients has shown that approximately 35% of the study population were given a single bolus, or double bolus, without the required maintenance infusion. These regimens resulted in significant under-dosing of bivalirudin and were associated with an increased incidence of Major Adverse Cardiac Events (MACEs).

This practice is a significant concern, and we have shared our concern with the relevant European Regulatory Agencies, who are in agreement with this communication to highlight the importance of adhering to the approved dosing regimen for Angiox®.

Further information

Administration of a bolus of 0.75mg/kg bivalirudin results in rapid attainment of therapeutic plasma concentrations. However, a subsequent infusion of 1.75 mg/kg/hour is necessary to maintain appropriate therapeutic concentrations for at least the duration of the PCI procedure so that anti-thrombin activity is sustained until satisfactory blood flow is re-established in the coronary artery and instrumentation of the coronary arteries is completed.

Reporting suspected adverse drug reactions

Please report suspected adverse reactions to Angiox® directly to Nycomed Limited (telephone 0353 642 0021) or to the Irish Medicines Board in the usual way.

Should you need additional information or have any comments or concerns regarding this matter, please contact Nycomed Limited (telephone 0353 642 0021).

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Yours faithfully

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