Malta, 06 February 2006

Circular No. P03/2006

Dear Healthcare Professional,

Re: Recent Study on Safety of Trasylol® (aprotinin)

Following discussion of a recent study[1] examining the safety of three agents used to prevent excessive blood loss in cardiac surgery (aprotinin, aminocaproic acid and tranexamic acid) at the Pharmacovigilance Working Party held at the European Medicines Agency (EMEA), the Medicines Authority is issuing this statement in order to provide some background information on this study and the action being taken at a European level.

Aprotinin is used to prevent major blood loss during cardiac surgery, and is also indicated in a limited number of other conditions associated with an increased risk of bleeding. It acts largely to reduce the breakdown of clots, which can lead to bleeding. The product information for aprotinin includes warnings about the risk of adverse cardiovascular events (including heart attacks) and renal impairment and failure.

The above-mentioned study conducted at the Ischemia Research and Education Foundation, US, was a very large multi-national, multi-centre obervational study comparing outcomes in patients undergoing cardiac surgery for either (a) elective coronary artery revascularisation or (b) complex cardiac surgery who received either: - no antifibrinolytic treatment (1374 patients) - aprotinin - aminicaproic acid (883) - tranexamic acid (822). The authors collected a large amount of data on each patient in order to correct for different risk factors that might be encountered. The results showed that aprotinin was associated with a significantly increased risk (versus control/no treatment) of renal failure requiring dialysis (in elective and complex surgery groups), and of heart attack (myocardial infarction), heart failure, stroke and encephalophaty (in the elective coronary patients group). Other treatments were not associated with an increased risk versus no treatment. All treatments were effective in reducing blood loss. The authors conclude that the use of aprotinin is unwise.

[1] Mangano, D. T., Tudor, I. C., Dietzel, C. (2006). The Risk Associated with Aprotinin in Cardiac Surgery. *NEJM* 354:353-365

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In response to this study, a Europe-wide review of the new data has been initiated. The Medicines Authority will closely follow this review and inform prescribers and patients about any new advice to emerge following the assessment of this study. In the meantime, prescribers are advised to weigh the benefits against the risks of aprotinin when prescribing to patients, as is the common practice when prescribing all medicinal products.