



Bayer HealthCare
Pharmaceuticals

IMPORTANT TRASYLOL SAFETY INFORMATION

October 25, 2007

Dear Health Care Professional:

Bayer HealthCare would like to inform you that the company has recently received important information from the Canadian-based BART Trial concerning the safety of Trasylo[®] (aprotinin injection).

Late last week, Bayer, the U.S. Food and Drug Administration (FDA), and Health Canada were notified that the BART Executive Committee had halted the Canadian-based trial. This followed a letter from the BART Data Safety Monitoring Board informing the Committee that a planned periodic data analysis indicated reduced bleeding but also an increase in all-cause mortality (that almost reached conventional statistical significance for 30-day mortality) in the aprotinin arm compared to patients who received either aminocaproic acid or tranexamic acid. Bayer immediately communicated this information to other health authorities around the world. Data have not, as yet, been shared with Bayer or regulatory authorities.

The BART study -- Blood Conservation using Antifibrinolytics: A Randomized Trial in High-Risk Cardiac Surgery Patients -- is a multi-institutional, blinded, randomized controlled trial to compare the efficacy and safety of the use of aprotinin, aminocaproic acid and tranexamic acid in approximately 3000 high-risk cardiac surgical patients undergoing either re-operation for coronary heart bypass graft (CABG) or aortic valve replacement, or combined valves or valve/CABG procedures. [For information on the BART Trial, visit www.ohri.ca/programs/clinical_epidemiology/thrombosis_group/studies/BART.asp]. The BART Trial has not been sponsored by Bayer and responsibility for the final analysis and release of BART data lies exclusively with the Canadian study investigators.

Bayer has also been informed that data will now be collected from all centers throughout Canada and data analysis will be undertaken by those conducting the BART study -- a process that is expected to take between four and eight weeks. Consequently no further evaluation either by Bayer or by regulatory authorities can take place until additional information becomes available from the BART investigators.

While the BART investigators collect and analyze the trial data, Bayer is providing guidance for physicians and other health care professionals that Trasylol be used only in accordance with approved product labeling. Trasylol is indicated for prophylactic use to reduce perioperative blood loss and the need for blood transfusion in patients undergoing cardiopulmonary bypass in the course of coronary artery bypass graft surgery who are at an increased risk for blood loss and blood transfusion.

Additionally, when deciding to prescribe Trasylol, physicians and health care professionals should also take into consideration that the BART Trial has been halted due to an increase in all-cause mortality (that almost reached conventional statistical significance for 30-day mortality) in patients in the aprotinin treatment arm compared to patients who received either aminocaproic acid or tranexamic acid.

Bayer has posted information and this letter to Health Care Professionals on its websites today www.trasylol.com, www.pharma.bayer.com, www.bayerscheringpharma.de/trasyslol/en, www.bayerhealthcare.com/trasylol/en. In the next days Bayer will mail a letter to health care providers around the world who use the product e.g. cardiothoracic surgeons, anesthesiologists and hospital pharmacists. Bayer has also been informed that the FDA plans to communicate with the public on this issue.

Patient safety remains Bayer's primary concern. Bayer believes Trasylol remains a safe and effective treatment option for physicians. Bayer will continue to work closely with the FDA, medical experts and health authorities in countries where Trasylol is marketed to re-evaluate the overall risk-benefit of the product and will evaluate the need for a label change and/or other actions as additional data and analyses become available from the BART trial.

If you wish to request further information, please contact your local Bayer HealthCare Medical Department.

Sincerely

Kemal Malik, MD
Head of Global Development, Member of the Board of Management
Bayer HealthCare Pharmaceuticals

About Trasylol

Important Safety Considerations

Trasylol® administration may cause fatal anaphylactic or anaphylactoid reactions. Fatal reactions have occurred with an initial (test) dose as well as with any of the components of the dose regimen. Fatal reactions have also occurred in situations where the initial (test) dose was tolerated. The risk for anaphylactic or anaphylactoid reactions is increased among patients with prior aprotinin exposure and a history of any prior aprotinin exposure must be sought prior to Trasylol® administration. The risk for a fatal reaction appears to be greater upon re-exposure within 12 months of the most recent prior aprotinin exposure. Trasylol® should be administered only in operative settings where cardio-pulmonary bypass can be rapidly initiated. The benefit of Trasylol® to patients undergoing primary CABG surgery should be weighed against the risk of anaphylaxis associated with any subsequent exposure to aprotinin.

(See CONTRAINDICATIONS, WARNINGS and PRECAUTIONS in the prescribing information.)

Safety Considerations

Trasylol is contraindicated in patients with a known or suspected aprotinin exposure during the last 12 months. Aprotinin may also be a component of some fibrin sealant products.

In clinical studies, hypersensitivity and anaphylactic reactions were rare (<0.1%) in patients with no prior exposure to Trasylol.

Trasylol administration increases the risk for renal dysfunction and may increase the need for dialysis in the perioperative period.

This risk may be especially increased for patients with pre-existing renal impairment or those who receive aminoglycoside antibiotics or drugs that alter renal function.

The incidence of serum creatinine elevations >0.5 mg/dL above pre-treatment levels was statistically higher in the high-dose aprotinin group (9.0%) compared with placebo (6.6%).

The incidence of serum creatinine elevations >2.0mg/dL above baseline was slightly higher in the high-dose aprotinin group (1.1% vs. 0.8%).

In clinical trials Trasylol® did not increase the risk of the following perioperative events: myocardial infarction, congestive heart failure, hepatic dysfunction and mortality.

For Trasylol® contraindications, warnings and precautions see prescribing information.