

## **Bayer Issues Additional Guidance to Physicians on Trasyolol®**

**Leverkusen, Germany and West Haven, CT, USA, October 25, 2007** – Today Bayer announced new guidance to physicians and health care providers regarding the use of Trasyolol® (aprotinin injection) in patients at an increased risk of blood loss and blood transfusion undergoing coronary artery bypass graft (CABG) surgery with cardiopulmonary bypass (CPB).

The company did so after being notified that the BART Executive Committee had halted the Canadian-based trial – a randomized, controlled trial being conducted in high-risk cardiac surgery patients. 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) for patients in the aprotinin treatment arm compared to patients who received either aminocaproic acid or tranexamic acid. Data have not, as yet, been shared with Bayer.

Bayer immediately informed the U.S. Food and Drug Administration (FDA), Health Canada and other health authorities around the world.

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.

Guidance from Bayer includes a recommendation that physicians use Trasyolol only in accordance with approved product labeling. Trasyolol 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 Trasyolol, physicians should also take into consideration that the BART Trial has been halted due to an increase in all-cause mortality in patients in the aprotinin treatment arm compared to patients who received either aminocaproic acid or tranexamic acid.

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 medical experts, the FDA 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.

Bayer has posted information regarding this issue on its websites [www.trasylol.com](http://www.trasylol.com), [www.pharma.bayer.com](http://www.pharma.bayer.com), [www.bayerscheringpharma.de/trasyslol/en](http://www.bayerscheringpharma.de/trasyslol/en), [www.bayerhealthcare.com/trasylol/en](http://www.bayerhealthcare.com/trasylol/en). Subsequently, in consultation with the FDA and other health authorities, the Company will issue a letter to health care providers who use Trasylol such as cardiothoracic surgeons, anesthesiologists and hospital pharmacists. Bayer has also been informed that the FDA plans to communicate with the public on this issue.

### **About BART**

According to information on the website of the Ottawa Health Research Institute (Institut de recherche en santé d'Ottawa), 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 study, visit: [www.ohri.ca/programs/clinical\\_epidemiology/thrombosis\\_group/studies/BART.asp](http://www.ohri.ca/programs/clinical_epidemiology/thrombosis_group/studies/BART.asp)

### **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.**

### **About Bayer HealthCare Pharmaceuticals Inc.**

Bayer HealthCare Pharmaceuticals Inc. is the U.S.-based pharmaceuticals unit of Bayer HealthCare LLC, a division of Bayer AG. One of the world's leading, innovative companies in the healthcare and medical products industry, Bayer HealthCare combines the global activities of the Animal Health, Consumer Care, Diabetes Care, and Pharmaceuticals divisions. In the U.S., Bayer HealthCare Pharmaceuticals comprises the following business units: Women's Healthcare, Diagnostic Imaging, Specialized Therapeutics, Hematology/Cardiology and Oncology. The company's aim is to discover and manufacture products that will improve human health worldwide by diagnosing, preventing and treating diseases.

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Forward-Looking Statement

*This news release contains forward-looking statements based on current assumptions and forecasts made by Bayer Group management. Various known and unknown risks, uncertainties and other factors could lead to material differences between the actual future results, financial situation, development or performance of the company and the estimates given here. These factors include those discussed in our annual and interim reports filed with the Frankfurt Stock Exchange. The company assumes no liability whatsoever to update these forward-looking statements or to conform them to future events or developments.*