

## **FDA Advisory Committees Recommend Continued US Marketing Authorization for Trasylol**

**Committees also recommend further changes to US Label for Trasylol and additional safety studies**

**Leverkusen, Germany; West Haven, CT, USA, September 12, 2007** -- Today, the Cardiovascular and Renal Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee to the U.S. Food and Drug Administration (FDA) held a meeting to discuss the risk /benefit profile of Trasylol® (aprotinin injection), a Bayer drug used in coronary artery bypass graft (CABG) surgery. At the close of the meeting, based on the Trasylol data in Bayer's controlled clinical studies and after considering data from observational studies and public testimony presented at the meeting, the Committees recommended that US marketing authorization for Trasylol should be continued.

The Committees also recommended that Bayer amend the U.S. product label for Trasylol to provide additional prescribing guidance to physicians and also recommended that Bayer conduct additional clinical studies, including randomized controlled trials, to further assess the risk and benefit of Trasylol.

Bayer was pleased to participate in today's session because it provided a proper forum in which to discuss the complex scientific issues surrounding the risk/benefit profile of Trasylol in detail. Trasylol is the only drug currently approved by the FDA 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.

Patient safety is Bayer's first and foremost concern. In line with the discussions and guidance received from the Committees today, the company will work with FDA on appropriate U.S. label revisions providing additional prescribing guidance to physicians.

The Committees also recommended that Bayer undertake additional clinical studies, including randomized controlled clinical trials, to further assess risks and benefits of Trasylol. Following the Committees' recommendation, Bayer will move forward with discussions with the FDA to reach agreement with them regarding further clinical activities.

Bayer is in close contact with other regulatory authorities around the world and will inform them of the outcome of today's meeting and potential next steps.

Bayer considers the discussion today and the valuable feedback provided by the Committees as important guidance and input that will help the company in clarifying and addressing these critical issues. Bayer continues to believe that the totality of the medical evidence, including the RCTs and other data discussed today demonstrates that Trasylol is safe and effective when used according to the product labeling. Bayer will continue to work closely and cooperatively with all regulatory authorities to address questions regarding safe and effective use of its drugs.

## 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.**

Press Contacts:

Michael Diehl, tel. +1 0049 214 30 585 32  
michael.diehl@bayerhealthcare.com

Meredith Fischer, tel. +1 203 812-6485  
meredith.fischer@bayer.com