



“The Risk of Aprotinin in Cardiac Surgery”

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Aprotinin Is Proven Unsafe, Doubling Risk Of Kidney Failure Drug Has Been Marketed for 13 Years; One Million Patients Exposed

Aprotinin’s Dangers

- In patients undergoing primary,* repeat, or complex* coronary artery surgery, aprotinin **doubles the risk of renal (kidney) failure**, requiring dialysis.
- An estimated **10,000 patients** are unnecessarily on dialysis today due to aprotinin use.
- In addition to renal failure, aprotinin was associated with an increased risk (among 3,013 primary surgery patients*), for:
 1. Myocardial infarction (heart attack) - **48 percent**
 2. Heart failure - **109 percent**
 3. Stroke/encephalopathy - **181 percent**.
- Replacement of aprotinin with safe, generic e-aminocaproic acid (1/100 the cost of aprotinin) would:
 1. Avoid **11,050** dialysis complications per year.
 2. Save **\$US 1 billion per year** in healthcare (dialysis) costs.
 3. Save **\$US 250 million per year** in drug costs.
- Replacement of aprotinin with safe, generic tranexamic acid (1/15 the cost of aprotinin) would avoid **9,790** dialysis complications each year, yielding similar direct and indirect savings.

**Patients were classified as primary surgery (3,013) if the index surgery was elective and coronary artery only, with no history of cardiac or vascular surgery, or angioplasty. Otherwise, patients were classified as complex surgery (1,361).*

Aprotinin Background

- Aprotinin is a drug used to reduce bleeding during cardiac surgery. Worldwide, it is among the three antifibrinolytic agents used in the majority of the **one million cardiac surgeries per year**.

- Aprotinin therapy is at least ten times as expensive as treatment with (generic) ε-aminocaproic or tranexamic acid. Both are safe, effective alternatives to aprotinin.

Bayer Healthcare Pharmaceuticals

- Aprotinin is manufactured by Bayer Healthcare Pharmaceuticals, under the brand name Trasylo1, and was approved by the U.S. Food and Drug Administration (FDA) in 1993.
- Bayer has extensively marketed Trasylo1.
- **In 2005, Trasylo1 sales rose 87 percent** during the 2nd quarter and **31 percent** in the 3rd quarter.

Bayer forecasts sales of Trasylo1 to be approximately **\$US 606 million in 2006**, tripling since 2004 (**\$US 213 million**).

Study Background

- Approximately **7,500** data fields were collected from **4,374 patients** by independent, investigators using a systematic sampling scheme at 69 of the world's leading cardiac centers and institutions in North and South America, Europe, the Middle East and Asia.
- Among 4,374 patients undergoing revascularization in the study, patients either received no antifibrinolytic, or one of the three antifibrinolytics (aprotinin, ε-aminocaproic acid or tranexamic acid).
- Breakdown of treatment patients received:
 - **1,374** patients were not given antifibrinolytic during surgery
 - **1,295** patients received aprotinin
 - **883** patients received ε-aminocaproic acid
 - **822** patients received tranexamic acid
- **The nonprofit Ischemia Research and Education Foundation**, a California-based, independent, nonprofit biomedical research organization, provided all of the funding for the study, totaling more than **\$US 35 million**.
- The nonprofit *McSPI* Research Group, a consortium of the leading surgery centers throughout the world, contributed an equivalent amount in collecting the vast amount of data.
- None of the authors received direct or indirect support from any of the manufacturers of these three drugs.
- The current finding is Dr. Mangano's and IREF-*McSPI*'s fourth major therapeutic discovery in the past decade.
 - In 1996, Mangano reported that generic beta-blockers reduced death after major surgery, saving 250,000 lives a year at a cost of \$15 per patient (*New England Journal of Medicine*).
 - In 2002, IREF-*McSPI* research found that giving heart patients aspirin immediately following surgery reduced the threat of thrombosis (*New England Journal of Medicine*).
 - In 2003, IREF-*McSPI* reported for the first time that the COX-2 inhibitor, Bextra (valdecoxib, parecoxib), was associated with stroke and impaired wound healing, eventually leading to its recall (*Journal of Thoracic and Cardiovascular Surgery*).