DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
1401 Rockville Pike
Rockville, MD 20852-1448

January 25, 1999

IMPORTANT DRUG WARNING

Dear Healthcare Provider:

The purpose of this letter is to inform you of important safety information regarding the use of Abbokinase (Urokinase). This information is intended to help physicians and patients understand the potential risks of transmitting infectious agents associated with the use of this product. **The FDA is recommending that Abbokinase be reserved for only those situations where a physician has considered the alternatives and has determined that the use of Abbokinase is critical to the care of a specific patient in a specific situation.**

During recent inspections of Abbott Laboratories and its supplier of the human neonatal kidney cells used in the manufacture of Abbokinase, the United States Food and Drug Administration (FDA) identified numerous significant deviations from the Current Good Manufacturing Practice regulations designed to help assure product safety.

Abbokinase is produced from primary cultures of kidney cells harvested post-mortem from human neonates. Products manufactured from human source materials have the potential to transmit infectious agents. While some procedures to help control such risks in products of human source are in place, recent manufacturing inspections revealed deficiencies in some of the procedures used by Abbott and its supplier of the human neonatal kidney cells that could increase the risk of transmitting infectious agents. In considering this risk, the prescriber should be aware of the following information regarding currently available lots of Abbokinase:

- The kidney cells used in the manufacture of this product were harvested post-mortem from human neonates from a population at high risk for a variety of infectious diseases, including tropical diseases. The screening of potential donors did not include the questioning of the mothers to determine infectious disease status or specific risk factors for infectious diseases. Although some efforts were made by Abbott's supplier to screen and test the mothers, neonate donors, and kidney cells, Abbott's testing of the materials it received indicates that these measures were not consistently or reliably performed.

- Neither the mothers nor the neonate donors were tested for hepatitis C virus (HCV) infection. Abbott has recently instituted a test for HCV in the kidney cells used in the manufacture of Abbokinase and negative test results have been obtained for currently available lots. However, Abbott has not validated this test.

- Prior to use in the manufacture of Abbokinase, the human kidney cells were harvested, stored and handled in a manner which may have permitted contamination with infectious agents.

- A viral inactivation procedure that substantially inactivates HIV and HCV in other biological products was used in the production of the currently available lots of Abbokinase. This process has variable effects on other infectious agents and has not been fully validated for viral inactivation of Abbokinase.

The FDA is not aware of any cases of infectious diseases that can be attributed to the use of Abbokinase. However, the likelihood that cases of infectious diseases caused by Abbokinase, if any, would have been recognized as such and reported to FDA is probably very low. Therefore, the actual risk to patients of developing an infectious disease as a result of using Abbokinase is unknown. For each setting in which the use of Abbokinase is being contemplated, we encourage you to consider the appropriateness of other treatment options. FDA approved indications for Abbokinase are: pulmonary embolism, coronary artery thrombosis, and i.v. catheter clearance. It should also be noted that the FDA has not approved the use of Abbokinase for clearance of peripheral venous and arterial obstructions or for clearance ofarterio-venous cannulae.

Other thrombolytic products on the U.S. market with well-described experience in multiple indications include Streptase® (Streptokinase), Kabikinase® (Streptokinase), Activase® (Alteplase), Eminase® (Anistreplase), and Retavase® (Reteplase). We encourage all physicians to consider the appropriateness of other treatment options. The following is a list of FDA-approved indications for each of the other thrombolytic products currently available in the U.S.:

Streptase® (Streptokinase) [Hoechst Marion Roussel]-distributed by Astra USA
Acute evolving transmural myocardial infarction
Pulmonary embolism
Deep vein thrombosis
Arterial thrombosis or embolism
Occlusion of arteriovenous cannulae

Kabikinase® (Streptokinase) [Pharmacia & Upjohn AB]
Acute evolving transmural myocardial infarction
Pulmonary embolism
Deep vein thrombosis
Arterial thrombosis or embolism

Activase® (Alteplase) [Genentech, Inc.]
Acute myocardial infarction
Acute ischemic stroke
Pulmonary embolism

Eminase® (Anistreplase) [Wulfing Pharma GmbH]-distributed by Roberts Pharmaceutical Corporation
Acute myocardial infarction

Retavase® (Reteplase) [Centocor, Inc.]
Acute myocardial infarction

Abbott has committed to updating the labeling for Abbokinase to include the information regarding the potential risk for transmission of infectious diseases and to expeditiously correcting the deviations from Current Good Manufacturing Practice.

It is important that adverse experiences involving suspect infections following the administration of Abbokinase be included among those adverse events reported to Abbott Laboratories, Pharmaceutical Products Division, North Chicago, IL 60064, at 1-800-633-9110, or to the Agency via the MedWatch program by phone at 1-800-FDA-1088, by fax at 1-800-FDA-0178, via the MedWatch website at www.fda.gov/medwatch, or by mail (using postage-paid form) at MedWatch, HF-2, FDA, 5600 Fishers Lane, Rockville, MD 20852-9787. Health professionals and consumers should use the Form 3500 for adverse event/product problem reporting.

FDA will provide updated information on this product, as appropriate, via the Internet at http://www.fda.gov/cber. Information also will be available from the CBER voice information system at 1-800-835-4709, the CBER FAX information system at 1-888-CBER-FAX, and to subscribers of CBER's automated mailing system, CBERINFO. Prescribers are encouraged to consult these resources.

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and Research