Wyeth®

IMPORTANT DRUG WARNING

WARNING REGARDING BRONCHIAL ANASTOMOTIC DEHISCENCE INCLUDING FATAL CASES

Dear Health Care Provider:

Wyeth wishes to inform you about important safety information regarding the use of Rapamune® in *de novo* lung transplant patients. Wyeth has received post-marketed reports of bronchial anastomotic dehiscence, including fatal cases, in patients treated with Rapamune® in combination with tacrolimus and corticosteroids. Two centers have reported this serious adverse event in lung transplant recipients in whom this immunosuppressive regimen was initiated at the time of transplantation. At one center, four of fifteen (4/15) patients enrolled in an investigator-sponsored study developed bronchial anastomotic dehiscence; a fatal outcome was identified in three of these four patients. Further information regarding these patients will be published in *Transplantation* in 2003. The second center reported two cases of bronchial anastomotic dehiscence, one of which was fatal.

The safety and efficacy of Rapamune as immunosuppressive therapy has not been established in lung transplant patients, and, therefore, such use is not recommended.

The prescribing information for Rapamune® has been updated to include new information in the boxed **WARNINGS** section, which will read as follows:

Liver Transplantation – Excess Mortality, Graft Loss, and Hepatic Artery Thrombosis (HAT): The use of sirolimus in combination with tacrolimus was associated with excess mortality and graft loss in a study in de novo liver transplant recipients. Many of these patients had evidence of infection at or near the time of death.

In this and another study in de novo liver transplant recipients, the use of sirolimus in combination with cyclosporine or tacrolimus was associated with an increase in HAT; most cases of HAT occurred within 30 days post-transplantation and most led to graft loss or death.

Lung Transplantation – Bronchial Anastomotic Dehiscence:
Cases of bronchial anastomotic dehiscence, most fatal, have been reported in de novo lung transplant patients when Rapamune has been used as part of an immunosuppressive regimen.

The safety and efficacy of Rapamune® (sirolimus) as immunosuppressive therapy have not been established in liver or lung transplant patients and therefore, such use is not recommended.

Full prescribing information is enclosed.

Rapamune is indicated for the prophylaxis of organ rejection in patients receiving renal transplants. It is recommended that Rapamune be used in a regimen with cyclosporine and corticosteroids.

WARNING: Increased susceptibility to infection and the possible development of lymphoma and malignancy, especially of the skin, may result from immunosuppression. Only physicians experienced in the use of immunosuppressive therapy and the management of transplant patients should use Rapamune. Patients receiving the drug should be managed in facilities equipped and staffed with adequate laboratory and supportive medical resources. The physician responsible for maintenance therapy should have complete information requisite for the follow-up of the patient.

Serious adverse events or product problems should be reported to Wyeth Global Safety Surveillance and Epidemiology by FAX at (610) 989-5544 or by mail to GSSE, 201 King of Prussia Road, 6th Floor, Radnor, PA 19087.

Please share this information with your colleagues involved in the care of transplant patients. A copy of the prescribing information for Rapamune is enclosed for your reference. Please contact Wyeth Medical Affairs at 1-800-934-5556 with any questions or concerns.

Sincerely,

Victoria Kusiak, MD
Vice President
North American Medical Affairs