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Wyeth

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IMPORTANT SAFETY INFORMATION

Dear Doctor,

Wyeth wishes to inform you about important safety information regarding the use of Rapamune® (sirolimus) 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 developed bronchial anastomotic dehiscence; a fatal outcome was identified in three of these four patients[1].

Wyeth wishes to draw your attention to the following:

- Cases of bronchial anastomotic dehiscence, some fatal, have been reported in de novo lung transplant patients when sirolimus has been used as part of an immunosuppressive regimen.

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

Rapamune is indicated for the prophylaxis of organ rejection in adult patients at low to moderate immunological risk receiving a renal transplant. It is recommended that Rapamune be used initially in combination with cyclosporine microemulsion and corticosteroids for 2 to 3 months. Rapamune may be continued as maintenance therapy with corticosteroids only if cyclosporine can be progressively discontinued. Increased susceptibility to infection and the possible development of lymphoma and

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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 through your local Wyeth representative.

Please share this information with your colleagues involved in the care of transplant patients. Please contact your local Wyeth representative with any questions or concerns.

Yours sincerely,

Angela Ryan

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[1] Data on file.