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IMPORTANT DRUG WARNING

SUBJECT: Tuberculosis and Infections with Enbrel® (etanercept)

March 14, 2008

Dear Health Care Professional:

Amgen Inc. and Wyeth Pharmaceuticals have added a BOXED WARNING to the ENBREL US Prescribing Information (US PI) to further strengthen and clarify information regarding the risk of infections, including tuberculosis (TB) in patients taking ENBREL; namely the new recommendation to screen for latent tuberculosis infection before beginning Enbrel. The complete BOXED WARNING is as follows:

WARNING
RISK OF INFECTIONS
Infections, including serious infections leading to hospitalization or death, have been observed in patients treated with ENBREL® (see **WARNINGS** and **ADVERSE REACTIONS**). Infections have included bacterial sepsis and tuberculosis. Patients should be educated about the symptoms of infection and closely monitored for signs and symptoms of infection during and after treatment with ENBREL®. Patients who develop an infection should be evaluated for appropriate antimicrobial treatment and, in patients who develop a serious infection, ENBREL® should be discontinued.

Tuberculosis (frequently disseminated or extrapulmonary at clinical presentation) has been observed in patients receiving TNF-blocking agents, including ENBREL®. Tuberculosis may be due to reactivation of latent tuberculosis infection or to new infection. Data from clinical trials and preclinical studies suggest that the risk of reactivation of latent tuberculosis infection is lower with ENBREL® than with TNF-blocking monoclonal antibodies. Nonetheless, postmarketing cases of tuberculosis reactivation have been reported for TNF blockers, including ENBREL®. Patients should be evaluated for tuberculosis risk factors and be tested for latent tuberculosis infection prior to initiating ENBREL® and during treatment. Treatment of latent tuberculosis infection should be initiated prior to therapy with ENBREL®. Treatment of latent tuberculosis in patients with a reactive tuberculin test reduces the risk of tuberculosis reactivation in patients receiving TNF blockers. Some patients who tested negative for latent tuberculosis prior to receiving ENBREL® have developed active tuberculosis. Physicians should monitor patients receiving ENBREL® for signs and symptoms of active tuberculosis, including patients who tested negative for latent tuberculosis infection.

The **ADVERSE REACTIONS: Infections** section of the US PI has also been updated to include the following information: "In global clinical studies of 20,070 patients (28,308 patient-years of therapy), tuberculosis was observed in approximately 0.01% of patients. In 15,438 patients (23,524 patient-years of therapy) from clinical studies in the US and Canada, tuberculosis was observed in approximately 0.007% of patients. These studies include reports of pulmonary and extra-pulmonary tuberculosis (see **WARNINGS**)."

The ENBREL Patient Package Insert (PPI) is being converted to a Medication Guide. The Medication Guide is designed to provide important patient safety information and increase the awareness about the proper use of ENBREL. The Medication Guide will be distributed when a prescription for ENBREL is dispensed in the US.

A copy of the revised US PI is enclosed. Following approval by the FDA the Medication Guide will be available on Enbrel.com. We encourage you to review the full prescribing information and discuss the safety information with your patients.

To report adverse patient experiences or request further safety information on ENBREL, please contact Amgen's Medical Information Connection™ at 1-800-77-AMGEN. Alternatively, adverse events may be reported to FDA's MedWatch reporting system:

- by phone (1-800-FDA-1088), by facsimile (1-800-FDA-0178),
- online (https://www.accessdata.fda.gov/scripts/medwatch/) or
- mailed, using the MedWatch for FDA 3500 postage paid form, to the FDA Medical Products Reporting Program, 5600 Fishers Lane, Rockville, MD 20852-9787

Sincerely,

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