December 2006

IMPORTANT DRUG WARNING

UPDATED SAFETY INFORMATION

Dear Healthcare Professional:

Genentech, Inc. and Biogen Idec, Inc. would like to inform you of important new safety information regarding Rituxan® (rituximab).

- Two cases of progressive multifocal leukoencephalopathy (PML) resulting in death, have been reported in patients receiving Rituxan® for treatment of Systemic Lupus Erythematosus (SLE). Rituxan® is not approved for the treatment of SLE.

- Previously, cases of PML have been reported in patients with lymphoid malignancies during or up to one year after completion of Rituxan®. The majority of patients received Rituxan in combination with chemotherapy or as part of a hematopoietic stem cell transplant.

- Physicians treating patients with Rituxan should consider PML in any patient presenting with new onset neurologic manifestations, particularly in patients with SLE, or lymphoid malignancies. Consultation with a neurologist, brain MRI, and lumbar puncture should be considered as clinically indicated.

The current Rituxan package insert, which contains information on cases of PML in patients with hematologic malignancies, is enclosed for your reference.
We are working with the regulatory authorities to update the Rituxan® prescribing information.

Progressive multifocal leukoencephalopathy (PML) is a rare, progressive, demyelinating disease of the central nervous system that usually leads to death or severe disability. PML is caused by activation of the JC virus, a polyomavirus that resides in latent form in up to 80% of healthy adults. JC virus usually remains latent, typically only causing PML in immunocompromised patients. The factors leading to activation of the latent infection are not fully understood. There is no currently accepted screening test for PML.

PML has been reported in the literature in HIV- positive patients, immunosuppressed cancer patients (including those with hematologic malignancies), organ transplant recipients, and patients with autoimmune disease, including SLE, who were not receiving Rituxan. Abnormalities in T cells have been described as important for reactivation of JC virus and PML.

A description of cases of PML in patients with hematologic malignancies treated with Rituxan is included in the current US prescribing information (See WARNINGS: HBV Reactivation with Related Fulminant Hepatitis and Other Viral Infections). There are approximately 23 reports of PML patients with hematologic malignancies treated with Rituxan®; the majority of these patients received Rituxan® in combination with chemotherapy or as part of hematopoietic stem cell transplant. PML has also been reported in the literature in patients with hematologic malignancies receiving chemotherapy or as part of hematopoietic stem cell transplant, who were not receiving Rituxan®.

JC virus infection with resultant PML and death has been reported in 2 patients with SLE treated with Rituxan®. These patients had longstanding SLE with multiple courses of immunosuppressant therapy prior to receiving Rituxan®, however Rituxan monotherapy was the last treatment administered prior to the diagnosis of PML. Both patients were diagnosed with PML within 12 months of their last infusion of Rituxan®. PML has also been reported in the literature in patients with SLE receiving prednisone, azathioprine, cyclophosphamide, and other immunosuppressant agents and who were not receiving Rituxan®.

In patients who develop PML, Rituxan® should be discontinued and reductions or discontinuation of concomitant immunosuppressive therapy and appropriate treatment, including antiviral therapy, should be considered. There are no known interventions that can reliably prevent PML or adequately treat PML if it occurs.

Rituxan® is indicated for the treatment of patients with relapsed or refractory, low-grade or follicular, CD20-positive, B-cell, non-Hodgkin's lymphoma (NHL), and for the first line treatment of follicular, CD20-positive, B-cell NHL in combination with CVP

chemotherapy. Rituxan® is also indicated for the treatment of low-grade, CD20-positive, B-cell NHL in patients with stable disease or who achieve a partial or complete response following first-line treatment with CVP chemotherapy. Rituxan® is also indicated for the first-line treatment of diffuse large B-cell, CD20-positive, NHL in combination with CHOP or other anthracycline-based chemotherapy regimens. Rituxan® in combination with methotrexate is also indicated to reduce signs and symptoms in adult patients with moderately- to severely- active rheumatoid arthritis who have had an inadequate response to one or more TNF antagonist therapies. The safety and effectiveness of Rituxan ® for the treatment of SLE has not been established and SLE is not an FDA-approved indication.

Health care professionals should report any serious adverse events possibly associated with the use of Rituxan® to Genentech Drug Safety at 1-888-835-2555. Alternatively, this information may be reported to the FDA's MedWatch reporting system by phone (1-800-FDA-1088), facsimile (1-800-FDA-1078), online at the MedWatch website (www.fda.gov/medwatch), or mailed to MedWatch, HF-2, 5600 Fishers Lane, Rockville, MD 20852-9787.

If you have any questions regarding the use of Rituxan®, please call the Genentech Medical Information/Communications Department at 1-800-821-8590.

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