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# IMPORTANT DRUG WARNING
# NEW SAFETY INFORMATION

Dear Healthcare Professional:

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

- A case of progressive multifocal leukoencephalopathy (PML) leading to death has been reported in a patient with rheumatoid arthritis (RA) who received Rituxan in a long-term safety extension clinical study. This is the first reported case of PML in a Rituxan-treated patient with RA

The case of JC virus infection with resultant PML and death was reported in an RA patient treated with Rituxan and was diagnosed approximately 18 months after the last dose of Rituxan. This case was confounded by the patient's development of oropharyngeal cancer, which was treated with chemotherapy (a platinum containing regimen) and radiation therapy 9 months prior to the development of PML. The patient had longstanding RA treated with immunosuppressants and a complex medical and rheumatologic history including Sjogren's syndrome and undetectable complement C4 levels. Treatment for RA included methotrexate, steroids, and a TNF antagonist prior to Rituxan therapy; and methotrexate and steroids during and after Rituxan therapy.

The Rituxan package insert WARNING section on PML has previously noted reports of PML in patients with hematologic malignancies and autoimmune diseases for which Rituxan is not approved. It has been updated to reflect the case of PML in an RA patient treated with Rituxan and is enclosed for your reference [See WARNINGS and PRECAUTIONS: 5.4 Progressive Multifocal Leukoencephalopathy (PML)].

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

In patients who develop PML, Rituxan should be discontinued and reductions or discontinuation in 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.

PML has been reported in the literature in populations such as: HIV-positive patients, immunosuppressed cancer patients (including those with hematologic malignancies), organ transplant patients, and patients with autoimmune disease who were not receiving Rituxan.

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) as a single agent, and for the treatment of previously untreated follicular, CD20-positive, B-cell NHL in combination with CVP chemotherapy. Rituxan is indicated for the treatment of nonprogressing (including stable disease), low-grade, CD20-positive, B-cell NHL, as a single agent, following first-line treatment with CVP chemotherapy. Rituxan is also indicated for previously untreated 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 and slow the progression of structural damage in adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more TNF antagonist therapies.

Rituxan has been associated with fatal infusion reactions, tumor lysis syndrome (TLS), severe mucocutaneous reactions and progressive multifocal leukoencephalopathy (PML). Hepatitis B reactivation and cardiac arrhythmias and angina have also been observed. Patients should be closely observed for signs of infection if biologic agents and/or DMARDs other than methotrexate are used concomitantly. Common adverse reactions: hypertension, nausea, upper respiratory tract infection, arthralgia, pruritus, and pyrexia.

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) or the Med Watch website at 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 Genentech Medical Information/communications Department toll free at 1-800-821-8590.

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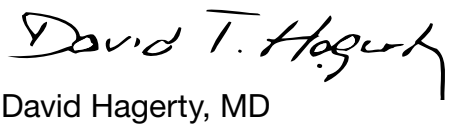

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