NATIONAL PBM COMMUNICATION
FDA MedWatch Information for Healthcare Professionals Regarding Rituximab and PML
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The Food and Drug Administration (FDA) and the manufacturers of rituximab (Rituxan®, Genentech) have reported one case of progressive multifocal leukoencephalopathy (PML) leading to death in a patient with rheumatoid arthritis (RA). This is the first reported case of PML in a rituximab–treated patient with RA. Consequently, the manufacturers have revised the "Warnings" section of the prescribing information for rituximab to reflect this specific case and have further highlighted the safety issue in a boxed warning. [1, 2, 3]

PML, a demyelinating disease of the central nervous system (CNS) caused by the JC polyomavirus (mainly seen in immunocompromised patients) has been associated with rituximab therapy. Previous product labeling cautioned about the reactivation of viral diseases, such as in PML, with the potential for severe disability or death. As of 2006, the FDA reported that approximately 23 cases of PML occurred in patients being treated with rituximab for hematologic malignancies. Fatal PML occurred in two patients after receiving treatment with rituximab for systemic lupus erythematosus (SLE). The first case appeared in a 70-year old female patient with a history of lupus nephritis and hemolytic anemia previously managed with cyclophosphamide, azathioprine, and various corticosteroids. Symptoms of vertigo, tongue biting, and difficulty walking appeared after 6 infusions of rituximab. An MRI revealed multiple brain lesions, and brain biopsy findings were consistent with PML. The second case involved a 45-year old female with a history of SLE, previously treated with cyclophosphamide and intravenous methylprednisolone. New neurological manifestations appeared after 3 infusions of rituximab. An MRI showed multiple brain lesions and cerebral spinal fluid tested positive for JC virus, confirming a diagnosis of PML. [4, 5]

The current FDA report describes one additional case of fatal PML in a patient receiving rituximab treatment for RA. PML was diagnosed in the patient approximately 18 months after the last dose of rituximab. The patient's medical history was significant for development of oropharyngeal cancer (treated with a platinum-including chemotherapy regimen and radiation 9 months before development of PML), long-standing RA treated with immunosuppressants (methotrexate, steroids, and a tumor necrosis factor inhibitor prior to receiving rituximab; and methotrexate and steroids during and after rituximab treatment), Sjogren's syndrome and undetectable complement C4 levels. [1, 2]

Both Genentech and the FDA recommend that healthcare providers prescribing rituximab should suspect PML in any patient who presents and develops new neurologic signs and symptoms. Consultation with a neurologist, brain MRI, and lumbar puncture should be considered as clinically indicated. [1, 2]

Any potential cases of PML in rituximab patients must be reported to FDA's MedWatch and VA ADERS program—please consult with local pharmacy staff if such an event occurs.

REFERENCES

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