

NATIONAL PBM COMMUNICATION

Biogen Idec Information for Healthcare Professionals Regarding Natalizumab and PML

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The manufacturers of natalizumab have reported a case of PML (progressive multifocal leukoencephalopathy) in the United States. This case was in a patient receiving monotherapy with natalizumab. Previous cases reported in August 2008 involved patients in Europe who were receiving monotherapy with natalizumab. The cases reported in 2005 involved three patients receiving natalizumab in addition to other immunosuppressive therapy.

Natalizumab was temporarily withdrawn from the market in 2005 because of the occurrence of three cases of PML. PML is a demyelinating disease of the CNS caused by the JC polyoma virus, which is mainly seen in immunocompromised patients. Two of the initial three cases occurred in patients being treated for multiple sclerosis (MS) and the third case of PML occurred in a patient receiving natalizumab for Crohn's disease.^{1,2} The reason for developing PML with natalizumab is still unknown. In an extensive evaluation of 3116 patients who had received natalizumab while participating in clinical trials, clinical history and examinations, MRIs, and testing of CSF for JC virus DNA were performed.³ Based on these evaluations, the investigators found that the estimated incidence of PML associated with exposure to natalizumab (with a mean exposure of 17.9 months) was 1.0 case per 1000 patients (95% CI, 0.2-2.8 per 1000).⁴ As of September 2008, there are approximately 35,000 persons that have received natalizumab globally. Of the total worldwide patients, 18,000 have received one year of natalizumab, 9,500 have been on for 18 months and 3,700 have been on for >24 months.

The current report describes an additional case of PML which has been reported in the United States. The patient had received 14 infusions of natalizumab. Diagnosis of PML was based upon the detection of JC Virus DNA in the cerebrospinal fluid (CSF) in the setting of clinical signs, symptoms and magnetic resonance imaging (MRI) findings consistent with the diagnosis of PML. The patient had a history of prior disease modifying therapies, including beta-interferons, glatiramer acetate and had methotrexate for a rheumatological condition.

To ensure close monitoring, all patients must enroll in the "TOUCH Prescribing Program" by completing an enrollment form. All patients must be thoroughly informed of the purpose and risk of natalizumab therapy, read and sign a detailed consent form. The patient must be evaluated by an informed health professional and sign a consent form before each monthly infusion. The TOUCH program provides specific guidelines for distinguishing PML from MS including MRI and cerebrospinal fluid assessment for JC virus DNA where PML might be considered.

The report of new cases of PML demonstrates the need for close monitoring and follow up of patients receiving natalizumab. Yearly MRI scans are recommended to detect the appearance of non-MS type lesions.

REFERENCES

1. Kleinschmidt-DeMasters BK, Tyler KL. Progressive multifocal leukoencephalopathy complicating treatment with natalizumab and interferon beta-1a for multiple sclerosis. *N Engl J Med* 2005; 353:369-374.
2. Langer-Gould A, Atlas SW, Green AJ, Bollen AW, Pelletier D. Progressive multifocal leukoencephalopathy in a patient treated with natalizumab. *N Engl J Med*. 2005 Jul 28;353(4):375-81
3. Van Assche G, Van Ranst M, Sciort R et al. Progressive multifocal leukoencephalopathy after natalizumab therapy for Crohn's disease. *N Engl J Med* 2005; 353:362-368
4. Yousry TA, Major EO, Ryschkewitsch C, et al. Evaluation of patients treated with natalizumab for progressive multifocal leukoencephalopathy. *NEJM*. 2006; 354(9):924-33