

FDA Public Health Advisory

Suspended Marketing of Tysabri (natalizumab)

FDA is issuing this public health advisory to inform patients and health care providers about the suspended marketing of Tysabri (natalizumab) due to two serious adverse events reported with its use. FDA has received a report from Biogen Idec, the manufacturer of Tysabri, of one confirmed, fatal case and one possible case of progressive multifocal leukoencephalopathy (PML) in patients receiving Tysabri for multiple sclerosis (MS). Both patients were enrolled in a long-term clinical trial and had been taking Tysabri for more than two years. There have been no previous cases of PML reported in patients taking Tysabri.

Although the relationship between Tysabri and PML is not known at this time, because of the rare, serious and often fatal nature of PML, FDA is announcing the following, effective immediately:

- ? Biogen Idec is voluntarily suspending marketing of Tysabri.
- ? Biogen Idec is suspending dosing of Tysabri in clinical trials and is notifying patients and investigators of the possible association between Tysabri and PML.

Patients being treated with Tysabri should contact their physician to discuss appropriate alternative treatments. At this time, there are no specific diagnostic or therapeutic interventions recommended for patients who have been taking Tysabri, other than to discontinue its use. Physicians should evaluate all patients who have received Tysabri and who have signs or symptoms suggestive of PML. Any suspect cases of PML should be reported immediately to Biogen Idec or to the FDA MedWatch program, as described at the end of this advisory. FDA and Biogen Idec will provide further guidance should additional recommendations be deemed appropriate.

Discussions between the FDA, Biogen Idec, and scientific experts have begun in order to assess the potential association between Tysabri and PML, methods for early diagnosis of PML, and to determine whether MS patients who may be at particular risk can be identified. These discussions will be informed by the substantial amount of patient data from clinical trials expected to be obtained in the next few months, including specific assessments of patients who have received Tysabri for evidence of early-stage PML, and will be used to guide decisions regarding future marketing of Tysabri.

PML is a rare, serious, progressive neurologic disease, usually occurring in immunosuppressed patients, often resulting in irreversible neurologic deterioration and death. There is no known effective treatment for PML, although reversing immune system suppression may slow or arrest progression of the disease.

Based on information submitted to the FDA this week, neither patient described above has known risk factors for PML. Both patients received concomitant Avonex (interferon beta-1a). The use of interferons, including Avonex, has not been associated with PML. To further understand the association between Tysabri and the development of PML, Biogen Idec is reviewing all adverse events in the clinical trial database for Tysabri to determine if any of these could possibly represent cases of PML.

Tysabri received accelerated approval in November 2004 for reducing the frequency of exacerbations in patients with relapsing-remitting MS, the most common form of this disease, after one year of treatment. Tysabri when added to Avonex reduced the risk of exacerbations by 54% compared to Avonex alone. Tysabri by itself reduced the risk by 66% compared to placebo. These results represent an important and meaningful benefit for patients with MS. At the time of approval, approximately 1,100 patients with MS had received Tysabri for one

year or more. Confirmatory studies were required to be carried out to show continued benefit of the drug after two years of treatment. The two cases reported here occurred in patients in the confirmatory studies. No cases of PML were observed during the clinical trials performed prior to approval of Tysabri.

The FDA will continue to notify health care providers and patients in a timely fashion as new information becomes available.

The FDA urges health care providers and patients to report adverse event information to FDA via the MedWatch program by phone (1-800-FDA-1088), by fax (1-800-FDA-0178), or by the Internet at

<http://www.fda.gov/medwatch/index.html>.