



National
Multiple Sclerosis
Society

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Expert Opinion Paper

National Clinical Advisory Board of the National Multiple Sclerosis Society

Treatment Recommendations for Physicians

Patient Access to Tysabri®

In June 2006, the U.S. Food and Drug Administration (FDA) approved the return to market of Tysabri (natalizumab), produced by Biogen Idec and Elan Pharmaceuticals, to delay the accumulation of physical disability and reduce the frequency of relapses (clinical exacerbations) in those with relapsing multiple sclerosis. The approval is based on positive results from two clinical trials showing that Tysabri significantly reduced the risk of sustained progression of disability and the rate of clinical relapse in those with relapsing MS.^{1,2}

The approval included creation of a mandatory registration program for patients and prescribing physicians, known as the TOUCH™ Program. The Food and Drug Administration describes the TOUCH Program as “a distribution program designed to assess the risk of progressive multifocal leukoencephalopathy (PML) associated with Tysabri, minimize the risk of PML, minimize death and disability due to PML, and promote informed risk-benefit decisions regarding TYSABRI use.” While it is not clear that TOUCH can actually reduce the risk of PML, or death and disability due to PML, the program should lead to a better understanding of the incidence of PML among MS patients exposed to TYSABRI. Of the three people in clinical trials involving Tysabri who developed PML, two died and one had permanent, serious neural damage. The drug, which is taken by monthly IV infusion, is only dispensed at registered infusion centers across the country.

The *Indications and Usage* section of the FDA-approved label for Tysabri reads as follows:

“Tysabri is indicated as monotherapy for the treatment of patients with relapsing forms of multiple sclerosis to delay the accumulation of physical disability and reduce the frequency of clinical exacerbations. . . . Tysabri is generally recommended for patients who have had inadequate response to, or are unable to tolerate, alternate MS therapies.”

Tysabri should not be used in combination with any other immunomodulatory agent, and is not recommended for individuals who have compromised immune systems.

Although the FDA has generally recommended Tysabri for use in patients with an inadequate response to other approved MS therapies, there is no present evidence-based standard for defining such an inadequate treatment response. This wording thus appears to give physicians considerable

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leeway in exercising their judgment when determining if Tysabri is an appropriate therapeutic option for a given patient. The Society's Expert Opinion Paper, "Changing Therapy in Relapsing Multiple Sclerosis" (http://www.nationalmssociety.org/docs/HOM/Exp_ChangTherapy.pdf), outlines several possible markers of treatment failure as guidance for clinicians.

The label's reference to "relapsing forms of MS" has been misconstrued and may benefit from clarification. The four Disease Course Classifications (Relapsing-Remitting MS, Secondary-Progressive MS, Primary-Progressive MS, and Progressive-Relapsing MS) represent the results of an international survey of disease patterns in MS³ and are now recognized worldwide as the standard approach to the description of MS at any stage. A relapse is conventionally defined as the development of new or recurring symptoms lasting at least 24 hours and separated from a previous attack by at least one month. The term "relapsing forms of MS" includes:

- ◆ Relapsing-Remitting MS (RRMS), which involves periodic relapses, followed by partial or complete recovery.
- ◆ Secondary-Progressive MS (SPMS) in those patients who were initially diagnosed with RRMS and convert to a course of steady progression several years later, but continue to have relapses.
- ◆ Progressive-Relapsing MS (PRMS), which is characterized by disease progression from onset with relapses superimposed along the way.

Patients in all three of these groups are considered candidates for Tysabri as long as they continue to have relapses. Patients with Primary-Progressive MS (which is progressive from onset and has no relapses) and those with SPMS and PRMS who are no longer experiencing relapses are not considered candidates for Tysabri. [NOTE: The term chronic progressive MS is outdated and no longer recognized.]

The Society encourages continued studies and analyses of existing data to help better predict favorable or unfavorable course of treatment. Until such time as additional evidence on Tysabri is available, decisions regarding the appropriate use of Tysabri should be made collaboratively—by the individual physician with expertise in MS and the patient—in order to ensure informed consent based on all known evidence of its safety and efficacy.

Clinicians are also encouraged to consider this Expert Opinion Paper, along with the Expert Opinion of the National Clinical Advisory Board entitled "Changing Therapies in Relapsing Multiple Sclerosis" as part of a process to determine a treatment plan.

REFERENCES

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