Address PML Symptoms

Efalizumab from page 1

Efalizumab Risk Advisory Issued

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Three confirmed cases and one possible case of progressive multifocal leukoencephalopathy in patients treated with efalizumab for psoriasis have triggered the Food and Drug Administration to issue a public health advisory.

In the advisory, the FDA warned that the cases of progressive multifocal leukoencephalopathy (PML)—a rare, usually fatal brain infection—occurred in patients aged 47-73 years treated with efalizumab (Raptiva) for moderate to severe plaque psoriasis for more than 3 years.

Two of the patients with confirmed PML and the patient with suspected PML died. None of the patients were on other immunosuppressive drugs. Efalizumab was approved for adults with moderate to severe plaque psoriasis in 2003.

The FDA advisory noted that the agency is reviewing information and will take appropriate steps to ensure that the risks of Raptiva do not outweigh its benefits; that patients prescribed Raptiva are clearly weighing its benefits; that patients treat their symptoms of PML; and that health care professionals carefully monitor patients for the possible development of PML.

According to the advisory, physicians should "carefully monitor patients on Raptiva, as well as those who have discontinued the drug, for any signs or symptoms of neurological disease, and periodically reassess the benefits of continued treatment."

"Patients should be familiar with the signs and symptoms of PML, and should be told to contact their health care providers immediately if they experience any of the symptoms." The association between PML and efalizumab was first reported by the FDA in October 2008 in a letter to health care practitioners. The letter noted that a 70-year-old man who had been treated with efalizumab for over 4 years was diagnosed with PML, and the drug was also suspected in a second case of PML in a 62-year-old man.

At that time, the agency announced that a boxed warning would be added to the label of efalizumab regarding the risk of PML. Other potentially fatal infections associated with treatment. The agency also announced that the manufacturer, Genentech Inc., had been asked to develop a Risk Evaluation and Mitigation Strategy (REMS) for the drug, which would include a patient medication guide distributed with each prescription (including refills) that would explain treatment risks.

“Take the risk of PML very seriously and are working diligently with the FDA to put the right plans in place that will help protect patient safety. We are evaluating all possible approaches to address the risk of PML with Raptiva use including a risk minimization plan. It is premature to disclose the scope of our plans until we’ve reached a formal agreement on these plans,” said in an interview, Dr. Craig L. Leonard, who has been involved with the research on efalizumab since 1999, said most dermatologists have been taking their patients off efalizumab, especially those who have been treated for more than 3 years.

It appears that this is a drug you cannot use safely over time,” said Dr. Leonard, who believes that the drug is the cause of PML, which does not seem to be related to the age of the patient, but more with the length of treatment.

“This is a very rare and devastating infection that is almost uniformly fatal and thus, as has been taken very seriously,” said Dr. Leonard of the department of dermatology at Saint Louis University. He disclosed that he is an adviser and speaker and has been an investigator for Genentech but owns no stock.

Only a handful of his patients opted to continue treatment after being apprised of the risk. Efalizumab is no longer available in an "extraordinary” circumstance where a patient with severe psoriasis cannot take a TNF-antagonist because of a history of multiple sclerosis, and they have failed TNF inhibitors and cyclosporine, and phototherapy and had no good options left, said Dr. Leonard.

The FDA advisory is available at www.fda.gov/cder/drug/advisory/efalizumab.htm. Possible cases of PML and other adverse events associated with the drug can be reported to the FDA’s MedWatch program at www.fda.gov/medwatch/index.html. A copy of Genentech’s letter is available at www.gene.com/products/information/immunological/raptiva/.