Pregabalin Is First Drug Approved for Fibromyalgia

BY ELIZABETH MECHCATIE
Senior Writer

Pregabalin has become the first drug to win approval by the Food and Drug Administration for the management of fibromyalgia.

The FDA based the approval on two double-blind, controlled trials of approximately 1,800 patients. Data from the studies have shown that patients with fibromyalgia "have decreased pain after taking [pregabalin], but, the mechanism by which [pregabalin] produces such an effect is unknown," according to an agency-issued statement.

In the clinical trials of patients with fibromyalgia, those on pregabalin (Lyrica) had "rapid and sustained improvements in pain," compared with those on placebo, and "reported feeling better and improvements in physical function," according to a statement issued by Pfizer, which manufactures pregabalin. The same statement explains that the drug's mechanism of action for fibromyalgia is not known, but states that patients with fibromyalgia may be more sensitive than normal to stimuli that are not usually painful, and that pregabalin may reduce the degree of pain experienced by patients with fibromyalgia by binding to a specific protein within "overexcited nerve cells."

The approval "marks an important advance, and provides a reason for optimism for the many patients who will receive pain relief" with pregabalin, Dr. Steven Galson, the director of the FDA's Center for Drug Evaluation and Research said in the FDA statement. He added, however, that consumers should understand that some patients in trials did not benefit from the drug, and that "we still have more progress to make for treatment of this disorder."

Side effects such as dizziness and sleepiness, blurred vision, weight gain, dry mouth, and swelling of the hands and feet seemed to be dose related.

The two studies enrolled patients diagnosed with fibromyalgia using American College of Rheumatology (ACR) criteria, which are a history of widespread pain for 3 months and pain present at 11 or more of the 18 specific tender point sites, according to the revised prescribing information for pregabalin. The two studies—a 14-week double-blind placebo-controlled study and a 6-month randomized withdrawal study—found that treatment was associated with a reduction in pain by visual analog scale and improvements based on a patient global assessment and on the Fibromyalgia Impact Questionnaire.

In the 14-week study, some patients experienced reductions in pain during the first week of treatment, which continued throughout the study. Nearly 70% of those on a total daily dose of 300 mg of pregabalin, and 78% of those on a total daily dose of 450 mg experienced any improvement on the patient global impression of change scale, compared with 48% of those on placebo. The total daily dose of 600 mg was not more effective than the lower doses, and there was evidence of dose-related side effects.

The daily dose should be administered in two divided doses per day, starting at a total daily dose of 150 mg/day, which may be increased to 300 mg/day, within 1 week; the maximum dose is 450 mg/day, according to the prescribing information.

The most common side effects in the trials were mild to moderate dizziness and sleepiness, blurred vision, weight gain, dry mouth, and swelling of the hands and feet also were also reported. Side effects appeared to be dose related, according to the FDA. Patients should talk to their physicians or other health care providers about whether pregabalin—which can impair motor function, concentration, and attention—can affect their ability to drive, the FDA advised. Pfizer has agreed to conduct a study of pregabalin in children and another in women who are breast-feeding.

Pregabalin, a centrally acting drug, was first approved in 2004 for the management of neuropathic pain associated with diabetic peripheral neuropathy and postherpetic neuralgia, and for the adjunctive therapy for adult patients with partial onset seizures. It is taken orally in capsule form. ■

Migraine Patients May Benefit From Magnesium or CoQ10

BY LESLIE SABBAGH
Contributing Writer

RANCHO MIRAGE, CALIF. — Alternative therapies are not a replacement for prescription drugs in migraine treatment, but they can reduce the severity of the attacks and help ease symptoms, reported Dr. Alexander Mauskop.

In fact, "anyone suffering from migraines can benefit from these treatments," Dr. Mauskop said. The most important point, he stressed at a meeting sponsored by the Diamond Headache Clinic, is that nonpharmacologic methods can be as effective as drugs, if not more effective. When instituting an alternative approach, the first step is to eliminate food triggers, encourage a proper sleep regimen, regular meal intake, and sufficient hydration.

Actual alternative therapies to control physiologic response to stress include regular aerobic exercise and biofeedback, said Dr. Mauskop, director of the New York Headache Center.

For migraines, the most commonly used supplements are magnesium, feverfew, coenzyme Q 10 (CoQ10), riboflavin, butterbur extract, and alpha lipoic acid.

The most important supplement, according to Dr. Mauskop, is magnesium. "It's known that up to 50% of people with acute migraine have a magnesium deficiency. … It is much more effective to treat them with a product they're deficient in rather than using drugs," he said. Magnesium is "very effective for 50% of those who are deficient in it, but even prescription drugs work for only 50% of migraineurs" (Headache 2003;43:601-10).

Research has found that, for migraine, CoQ10 at 300 mg/day is effective, and that for Parkinson's disease 1,200 mg/day is effective. "Riboflavin has similar function in the body as CoQ10 and was shown to prevent migraine in one double-blind study. Although the therapeutic amount of riboflavin is very high—400 mg/day; many multivitamins have only 2-3 mg," he said (Neurology 1996;50:440-66).

Butterbur, 50 mg t.i.d, has also been found to help treat migraine, most likely due to its anti-inflammatory properties, or "maybe something else. Herbal products contain hundreds of chemicals and we can only guess which are the active ones" (Neurology 2004;63:2240-4).

Dr. Mauskop recommends a combination of magnesium, feverfew, and riboflavin: "I find that about half of people are very happy with [this combination]. Sometimes their headaches completely disappear so that they don't need prescription drugs."

The triple combination, available as MigreLief, costs $18 per month, and "if money is not an issue, I add CoQ10." Patients take 300 mg/day of MigreLief for 8 weeks. Although one study that showed favorable results in migraine patients used 100 mg t.i.d., "I often recommend 300 mg once daily due to adherence issues."

Patients have a continuum of responses. "Some say their headaches are more responsive to prescription drugs and some have total disappearance of migraines, with most responses somewhere in the middle," he said.

Butterbur has only one manufacturer, Dr. Mauskop said, "but feverfew is sold by many companies and the products are not always of good quality. Patients need to buy recognized brands or the triple combination supplements." Dr. Mauskop is a paid consultant to Quantum, Inc., the manufacturer of MigreLief. ■

Look for Depression, PTSD in Iraq War Vets With Migraines

BY MARY JO M. DALES
Editorial Director

BOSTON — In soldiers returning from combat in Iraq, a self-reported history of migraine headaches was associated with at least twice the risk of symptoms of depression, posttraumatic stress disorder, and anxiety as was seen in similar soldiers without migraines, based on a study presented at the annual meeting of the American Academy of Neurology.

Migraines appear to be frequently associated with symptoms of psychiatric conditions in soldiers returning from deployment, Maj. Jay C. Erickson, MC, USA, said during a press conference at the meeting, where the study results were presented during a scientific poster session.

Although all soldiers returning from deployment undergo mental health screening, there is the possibility that headaches and symptoms of a psychiatric condition could present after such testing and possibly outside the Veterans Affairs health care system, he said. Mental health screening is warranted to assure that psychiatric disorders are identified and properly treated at that time.

Dr. Erickson of Madigan Army Medical Center at Fort Lewis in Tacoma, Wash., reported the findings from a health screening questionnaire completed by nearly 2,200 of 3,600 soldiers returning to Fort Lewis in Washington state after a 1-year combat duty deployment to Iraq. The questionnaires, completed within 90 days after the soldiers' return, indicated that nearly 20% had migraine headaches.

The study results are limited by their self-reported nature, which does not establish a diagnosis and is likely to result in more reports of symptoms; they also are limited by a lack of information about predeployment rates of migraine. Nevertheless, the rates are twice those seen in 20- to 40-year-olds in the general population and in men, who comprised 96% of the study participants.

Respondents answered 15 questions about the nature and frequency of any headaches in the last 3 months. They also completed the four-question Primary Care PTSD Screen (PC-PTSD) and the Patient Health Questionnaire (PHQ9) screen for depression and anxiety.

The responses indicated that 32% screened positive for depression, 22% for PTSD, and 9% for anxiety. Overall, 39% of respondents had at least one psychiatric condition. Respondents with migraines, compared with those without migraines, had much higher rates of depression symptoms (50% vs. 27%), symptoms of PTSD (39% vs. 18%), and anxiety symptoms (17% vs. 7%).

Migraine days per month were linked to a higher probability of a positive screen for depression and PTSD, but not a higher rate of anxiety symptoms. Those with migraine and depression symptoms had an average of 3.5 headaches days per month, compared with 2.5 days for those with migraine and no depression. ■