

# Ropinirole Approved for Restless Legs Syndrome

BY DAMIAN McNAMARA  
Miami Bureau

MIAMI BEACH — The antiparkinsonism drug ropinirole is now indicated for the treatment of adults with moderate to severe restless legs syndrome.

The Food and Drug Administration approved the new indication based on three randomized, double-blind, controlled trials that showed significant improvements in patient and physician symptom ratings, compared with placebo.

One of these studies showed that ropinirole (Requip, from GlaxoSmith-Kline) was well tolerated and effective at improving symptoms in as little as 1 week. Richard Bogan, M.D., presented results of this phase III study at the annual meeting of the American Academy of Neurology.

Restless legs syndrome is a sensorimotor neurologic disorder affecting 5%-10% of the U.S. population. The condition causes considerable sleep disturbance and impairs quality of life for some patients. Although the pathogenesis is unknown, dopamine agonists such as ropinirole may be effective as first-line treatment for moderate to severe cases, according to Dr. Bogan of the University of South Carolina.

To test safety and efficacy, Dr. Bogan and his colleagues randomized 187 patients to ropinirole and 193 others to placebo in a 12-week, double-blind, multicenter trial. All participants had mild to moderate impairment; entry requirements included an International Restless Legs Syndrome (IRLS) study group criteria score of 15 or more, at least 15 nights of symptoms in the last month, and 4 nights of symptoms in the last 7 nights.

"Patients do have changes in quality of life, and ropinirole can improve their lives," said Dr. Bogan, president and medical director of SleepMed Inc.

The primary measure of efficacy was change in IRLS score between baseline and the last clinical observation before the end of the 12-week trial. Secondary outcomes included the change in IRLS score from baseline to week 1 and the proportion of patients in each group with a score of "much improved" or "very much improved" at weeks 1 and 12 on the Clinical Global Impression-Improvement scale. In addition, researchers assessed sleep quantity and quality with the Medical Outcomes Study sleep scale.

All participants were adults, with a mean age of 52 years (range 18-79 years). Women accounted for 58% of the ropinirole group and 63% of the placebo group. A total of 164 ropinirole recipients and 167 placebo recipients completed the study.

The treatment group received once-daily ropinirole 0.25 mg at baseline, 1-3 hours before bedtime. Dosages were titrated up to 4.0 mg/day to optimize efficacy without side effects. Dr. Bogan has received research grants from GlaxoSmithKline, the sponsor of this study.

There were "highly statistically significant" improvements in patient subjective assessments on the IRLS scale, Dr. Bogan said. Ropinirole reduced IRLS scores a mean of 3.7 points, compared with 2.0 points for placebo, at the patient's last

clinical observation, which occurred either at 12 weeks or, in some cases, earlier.

Changes on the global impression scale "were highly statistically significant as well, although clearly, there is a placebo effect." The proportion of patients with a Clinical Global Impression score of "much" or "very much improved" was significantly higher for ropinirole than placebo at week 12 (2.1 adjusted odds ratio).

"I am frustrated by my inability to tease out the placebo effect, by the scales we

use, and the variability of their symptoms," Dr. Bogan said in response to a question from the audience.

Ropinirole was associated with symptom relief as early as the first week of treatment. IRLS scores dropped by 4.1 points in the drug group versus 2.7 points in the placebo group at the end of the first week. In addition, a significantly higher proportion of ropinirole participants had Clinical Global Impression improvements at week one (2.4 adjusted odds ratio).

The treatment also provided qualitative improvements in sleep. Measures of sleep adequacy and quantity showed patients on active therapy experienced "dramatic improvements, especially in quantity of sleep," Dr. Bogan said.

Ropinirole was generally well tolerated. The most common adverse events associated with ropinirole were nausea, headache, and somnolence. Nausea, for example, occurred in 42% of the treatment group, versus 8% of the placebo group. ■

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