Gabapentin Enacarbil Eases Symptoms in RLS

BY BRUCE JANCIN

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SAN ANTONIO — Long-term use of gabapentin enacarbil for treatment of restless leg syndrome does not lead to the symptom augmentation that commonly occurs with dopaminergic agents, a study shows.

The symptom augmentation study was but one of a flurry of clinical trials of the investigational drug for restless legs syndrome (RLS) presented at the meeting.

Gabapentin enacarbil is a once-daily oral prodrug of gabapentin with pharmacokinetics superior to the parent drug.

The RLS augmentation that occurs as an unwanted side effect of dopaminergic therapy consists of increased symptom severity, extension of symptoms to previously unaffected parts of the body, or onset of symptoms at least 2 hours earlier in the evening than before treatment.

Average symptom duration per evening in the treatment group fell by 52 minutes from a baseline of 102 minutes, and by 37 minutes from 112 minutes in the placebo group.

Dr. Richard K. Bogan reported on 427 patients with a mean 14-year history of RLS who were randomized double-blind to 12 weeks of gabapentin enacarbil at 1,200 mg or placebo once daily at 5 p.m. taken with food.

Mean scores on the International Restless Legs Scale (IRLS) in the gabapentin enacarbil group improved by 13.1 points from a baseline of 23, which was significantly better than the 9.3-point drop with placebo. The average duration of RLS symptoms per evening in the gabapentin enacarbil group decreased by 52 minutes from a baseline of 102 minutes, and by 37 minutes from a baseline of 112 minutes in placebo-treated patients.

There was no suggestion of RLS symptom augmentation with the investigational drug based on time to onset or duration of symptoms, according to Dr. Bogan, chairman and chief medical officer of SleepMed Inc. in Columbia, S.C.

Dr. Aaron L. Ellenbogen presented an open-label, 52-week extension study of 386 patients who were treated with gabapentin enacarbil. Mean IRLS scores improved from 23.2 at baseline to 8. The investigators rated 85% of the subjects as "responders" on the Clinical Global Impression-Improvement scale.

Gabapentin enacarbil was not associated with any increase in daytime sleepiness, a common side effect with pramipexole (Mirapex) and ropinirole (Requip), the dopamine agonists approved for treatment of RLS. Mean scores on the Epworth Sleepiness Scale in the open-label study went from 6.7 at enrollment to 5.7 after a year.

Eleven percent of patients withdrew because of an adverse effect, the most common of which were somnolence and dizziness, reported Dr. Ellenbogen of the Michigan Institute for Neurological Disorders, Farmington Hills, Mich.

Roughly 60% of patients report pain in association with their RLS, and one-third of them describe this as their most troublesome symptom. Gabapentin enacarbil effectively relieves this pain, according to Dr. Daniel O. Lee.

He reported on 321 patients with moderate to severe RLS who were randomized to gabapentin enacarbil at 1,200 or 600 mg or placebo once daily for 12 weeks. Sixty-nine percent of those on gabapentin enacarbil at 1,200 mg and 68% on 600 mg reported at least a 30% reduction from baseline in pain scores, compared with 52% on placebo.

Moreover, 60% of patients on 1,200 mg/day and 56% on 600 mg/day reported at least a 50% reduction in pain, compared with 44% on placebo, said Dr. Lee of East Carolina Neurology in Greenville, N.C.

XenoPort Inc., which is collaborating with GlaxoSmithKline Inc. in developing gabapentin enacarbil, supported the studies. Dr. Lee, Dr. Ellenbogen, and Dr. Bogan disclosed serving as consultants to numerous pharmaceutical companies, including GlaxoSmithKline. ■