OBSERVATIONS

Gabapentin Extended Release for the Treatment of Painful Diabetic Peripheral Neuropathy

Efficacy and tolerability in a double-blind, randomized, controlled clinical trial

A randomized, double-blind, placebo-controlled study was conducted in 147 patients to determine the efficacy and safety of gabapentin extended release (g-ER) in treating pain associated with diabetic peripheral neuropathy (DPN). Gabapentin, an immediate-release formulation, has demonstrated clinical efficacy in DPN patients but also a relatively high incidence of somnolence and dizziness at the doses required for effective treatment of DPN pain (1,2). Using the polymer-based AcuForm technology, g-ER tablets have been formulated to handle the saturable transport mechanism responsible for the lack of dose proportionality seen with gabapentin. When administered with a meal, g-ER tablets gradually expand and release the drug to the upper gastrointestinal tract over an extended period of time (3). This enables g-ER to be administered once or twice daily, versus three times daily or more (4) for regular gabapentin, while providing equivalent or improved bioavailability and potentially improving tolerability, convenience, and minimized incidence of adverse events.

In this clinical trial, g-ER was dosed as either a single dose in the evening or as an asymmetrically divided dose regimen with the larger dose in the evening. It was hypothesized that this would provide maximum pain relief at night, when it is most needed, and that the commonly observed adverse events of dizziness and somnolence would be less burdensome because they would be more likely to occur while the patient was asleep.

Patients with a clinical diagnosis of DPN were queried about symmetrical painful symptoms in distal extremities (minimum 1–5 years) and baseline average daily pain (ADP) score (≥4) using a questionnaire. Randomized patients received 3,000 mg g-ER, as either a single evening daily dose or a divided dose (1,200 mg in the morning and 1,800 mg in the evening), or placebo for 4 weeks. g-ER was rapidly titrated from 300 to 3,000 mg/day over 2 weeks, followed by two additional weeks at 3,000 mg/day. Efficacy measures included changes from baseline to end point in ADP and daily sleep interference scores.

Most patients were male (55.1%), white (68.7%), and type 2 diabetic (95.2%), with a mean DPN duration of 3.4 years and a mean age of 59 years. Baseline mean pain scores for patients in the g-ER single-dose and divided-dose groups and placebo were 6.8, 6.7, and 6.9, respectively. Neuropathic pain was most often reported in the foot.

A significant decrease in ADP score was observed in the g-ER single-dose group (−2.76; $P = 0.001$) versus the placebo group (−1.38). There were significantly more responders (≥50% decrease in ADP scores) in the g-ER single-dose group (41.3%; $P < 0.001$) than in the placebo group (11.8%). Similar results were observed for changes in daily sleep-interference scores. The incidence of adverse events commonly associated with g-ER was low: dizziness was reported in 17.0, 12.2, and 0% and somnolence in 12.8, 4.1, and 0% of patients in the g-ER single-dose, divided-dose, and placebo groups, respectively. We conclude that 3,000 mg g-ER taken once daily was effective and well tolerated for the treatment of DPN pain.

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