Peripheral Edema and Weight Gain in Adult Patients With Painful Diabetic Peripheral Neuropathy Receiving Gabapentin Enacarbil or Pregabalin Enrolled in a Randomized Phase 2 Trial

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Background

• Gabapentin enacarbil (GEn) is a prodrug of gabapentin that has been approved for the management of painful diabetic peripheral neuropathy (DPN). GEn is not approved for use in the treatment of diabetic peripheral neuropathy (DPN).

• This is the first study to compare edema and weight gain between all GEn doses and pregabalin (Preg) in a phase 2 trial.

• GEn is an actively transported prodrug of gabapentin that has been approved for the treatment of moderate-to-severe primary restless legs syndrome (RLS) in adults (600 mg once daily) by the United States FDA.

• GEn is not approved for use in the treatment of diabetic peripheral neuropathy (DPN).

• Across treatment groups, the majority of patients reported at least one TEAE. The most common TEAEs were somnolence, nausea, and peripheral edema.

• Differences in mean 24-hour average pain intensity score between GEn and placebo were:

• The observed differences in peripheral edema and weight gain between all GEn doses examined and pregabalin are of clinical significance, given that these TEAEs may lead to limitations in patients willingness to tolerate and adhere to prescribed medicines.

• GEn is approved for the management of RLS in adults once daily dose of 1200 mg. Additional benefit of using doses greater than 1200 mg efficacy was not demonstrated, and these higher doses resulted in an increase in adverse reactions.

Results

• At a total of 423 patients were randomized to the treatment arms. One patient in the GEn 3600 mg group was lost to follow-up and therefore was excluded from the safety population.5

• Randomized and baseline characteristics are shown in Table 1.

• Table 1. Baseline Characteristics of the Safety Populationa

• Table 2. Most Common Treatment-Emergent Adverse Events Reported in Adults With Painful Diabetic Peripheral Neuropathy During the Treatment Period

• In the phase 2 study of patients with nephropathic pain, GEn was associated with overall lower incidences of peripheral edema and weight gain compared with pregabalin.6

• The weight gain in GEn-treated patients appears to be dose-dependent.

• The observed differences in peripheral edema and weight gain between all GEn doses examined and pregabalin are of clinical significance, given that these TEAEs may lead to limitations in patients willingness to tolerate and adhere to prescribed medicines.

• GEn is approved for the management of RLS in adults once daily dose of 1200 mg. Additional benefit of using doses greater than 1200 mg efficacy was not demonstrated, and these higher doses resulted in an increase in adverse reactions.

Conclusions

• The observed differences in peripheral edema and weight gain between all GEn doses examined and pregabalin are of clinical significance, given that these TEAEs may lead to limitations in patients willingness to tolerate and adhere to prescribed medicines.

• GEn is approved for the management of RLS in adults once daily dose of 1200 mg. Additional benefit of using doses greater than 1200 mg efficacy was not demonstrated, and these higher doses resulted in an increase in adverse reactions.

References


Disclosures

• All authors receive personal or institutional stock in XenoPort, Inc.

• The study was sponsored by XenoPort, Inc. or XenoPort, Inc.

• All the authors and XenoPort, Inc. are employees of XenoPort, Inc.

• XenoPort, Inc.

• Efficacy and Safety of Gabapentin Enacarbil in Painful Diabetic Peripheral Neuropathy, a Randomized Phase 2a Study. Presented at the American Academy of Neurology, 2013

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Figure 1. Study Design

Figure 2. Incidence of Peripheral Edema in the Safety Population

Figure 3. Incidence of Weight Gain in the Safety Population

Figure 4. Mean Change From Baseline in Weight Gain at wk 15/16 (LOCF)7

Figure 5. Mean Change From Baseline in Weight Gain8

Table 1. Baseline Characteristics of the Safety Populationa

Table 2. Most Common Treatment-Emergent Adverse Events Reported in Adults With Painful Diabetic Peripheral Neuropathy During the Treatment Period

• All patients included in the randomized treatment arms, one patient in the GEn 3600 mg group was lost to follow-up and therefore was excluded from the safety population.

• Compared with pregabalin, patients randomized to GEn experienced less peripheral edema and weight gain (Figures 2 and 3).

• For example, 6 patients in the GEn 3600 mg group experienced the most weight gain, whereas in the 1200 mg group experienced the least weight gain.

• By week 5 and after 4 weeks of the maintenance treatment phase, patients in the pregabalin group had experienced a greater increase in weight from baseline (Figure 5). Mean body weight increased over time in all active treatment groups, although changes were smaller in the lower-dose GEn groups.

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American Academy of Neurology 60th Annual Meeting – Pennsylvania Convention Center, Philadelphia, PA – April 26–2 May 2014

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