

An overview of eslicarbazepine acetate (ESL) as adjunctive therapy for partial-onset seizures

Background: Eslicarbazepine acetate (ESL) is a voltage-gated sodium channel blocker chemically related to carbamazepine. Eslicarbazepine acetate is metabolized to eslicarbazepine, the pharmacologically active moiety, and unlike carbamazepine is not metabolized to epoxides or susceptible to autoinduction. ESL and glucuronide metabolites are renally excreted in humans.

Methods: Three Phase III double-blind, placebo-controlled trials were conducted in adults (n=1049) with ≥ 4 partial-onset seizures/month despite treatment with 1-3 other antiepileptic drugs (AEDs) (oxcarbazepine was not allowed). Subjects were randomized to once-daily ESL (400 mg, 800 mg, or 1200 mg) or placebo as adjunct therapy to their current AEDs. Data from the trials were pooled. The primary efficacy endpoint was 4-week standardized seizure frequency over the 12-week maintenance period.

Results: Seizure frequency was significantly lower relative to placebo following treatment with ESL 800 mg ($p < 0.0001$) and 1200 mg ($p < 0.0001$). Results of the secondary endpoints (median relative reduction in seizure frequency, responder rate) were consistent. The efficacy was similar between subjects regardless of the number and type of concomitant AEDs. The most common AEs were dizziness, somnolence, headache, nausea, diplopia, vomiting, and abnormal coordination. There were no systematic effects on serum lipids and cholesterol, liver enzymes, glucose, body weight, or ECG parameters. 0.5% of ESL-treated patients (4/760) had at least one serum sodium value < 125 mEq/L during treatment, compared to none of the patients receiving placebo. The incidence of serious dermatological reactions with ESL was low. Most observed events were mild or moderate in severity.

Conclusion: Once-daily administration of ESL 800 mg and 1200 mg as adjunctive therapy reduced partial-onset seizure frequency in adult patients currently receiving 1-3 concomitant AEDs. There were dose-related increases in mostly mild to moderate AEs during treatment with ESL.

Current stage of development: Three phase 3 clinical trials in adjunctive treatment for partial-onset seizures in adults are complete.

Potential future preclinical and clinical development plans: Further studies are planned to evaluate the efficacy and safety of ESL as monotherapy, and its use in pediatric populations with epilepsy.

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