

# Long-term safety of perampanel and seizure outcomes in refractory partial-onset seizures and secondarily generalized seizures: Results from phase III extension study 307

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*Epilepsia*, 55(7):1058–1068, 2014  
doi: 10.1111/epi.12643

## SUMMARY

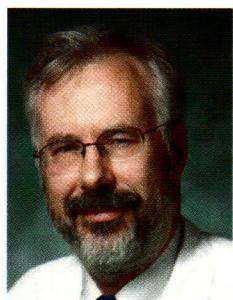
**Objective:** To evaluate safety, tolerability, seizure frequency, and regional variations in treatment responses with the AMPA antagonist, perampanel, in a large extension study during up to 3 years of treatment.

**Methods:** Patients ≥12 years old with partial-onset seizures despite treatment with 1–3 antiepileptic drugs at baseline completed a perampanel phase III trial and entered extension study 307 (NCT00735397). Patients were titrated to 12 mg/day (or their individual maximum tolerated dose) during the blinded conversion period, followed by open-label maintenance. Exposure, safety (adverse events [AEs], vital signs, weight, electrocardiography [ECG], laboratory values) and seizure outcomes were analyzed; key measures were assessed by geographic regions.

**Results:** Among 1,216 patients, median exposure was 1.5 years (range 1 week to 3.3 years), with >300 patients treated for >2 years. Treatment retention was 58.5% at cutoff. AEs reported in ≥10% of patients were dizziness, somnolence, headache, fatigue, irritability, and weight increase. Only dizziness and irritability caused discontinuation in >1% of patients (3.9% and 1.3%, respectively). The only serious AEs reported in >1% of patients were epilepsy-related (convulsion, 3.0%; status epilepticus, 1.1%). No clinically relevant changes in vital signs, ECG or laboratory parameters were seen. After titration/conversion, responder rate and median percentage change from baseline in seizure frequency were stable: 46% for both measures at 9 months (in 980 patients with ≥9 months' exposure) and 58% and 60%, respectively, at 2 years (in the 337 patients with 2 years' exposure). Median percentage reduction in frequency of secondarily generalized (SG) seizures ranged from 77% at 9 months (N = 422) to 90% at 2 years (N = 141). Among the 694 patients with maintenance data ≥1 year, 5.3% were seizure-free for the entire year.

**Significance:** No new safety signals emerged during up to 3 years of perampanel exposure in 39 countries. Seizure responses remained stable, with marked reductions, particularly in SG seizures.

**KEY WORDS:** Epilepsy, Antiepilepsy drugs, AMPA receptor, Antagonist, Seizure freedom.



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Accepted March 27, 2014; Early View publication May 27, 2014.

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