

## **Study Suggests Zonegran® (zonisamide) Capsules Are Not Likely to Reduce the Effectiveness of a Combination Oral Contraceptive**

### ***Zonegran Does Not Affect the Pharmacokinetics of OCs Containing EE and NOR***

(MIAMI BEACH, Fla.) – April 12, 2005 – New data presented today suggest Zonegran does not significantly reduce the effectiveness of oral contraceptives (OCs) that contain ethinyl estradiol (EE) and norethindrone (NOR), two common estrogen and progestin components of OCs. These findings are important because several commonly prescribed antiepileptic drugs (AEDs) may reduce the effectiveness of oral contraceptives, a potentially serious drug interaction for some women with epilepsy.

Findings from this single-center, open-label cross-over study were reported at a poster session at the American Academy of Neurology's 57th Annual Meeting. Zonegran is an AED approved by the U.S. Food and Drug Administration (FDA) as adjunctive therapy in the treatment of partial seizures in adults with epilepsy.

“The results of this study indicate that zonisamide may not affect the pharmacokinetics of the two drugs in a commonly prescribed oral contraceptive. This information can provide clinicians with greater confidence when prescribing zonisamide for women,” said James Cloyd, PharmD, College of Pharmacy, University of Minnesota.

The study, also recently published in *Clinical Therapeutics*, examined the effect of clinically relevant Zonegran maintenance doses on the pharmacokinetics (serum concentrations, distribution, and elimination) of EE and NOR, the two components of Ortho-Novum 1/35. Participants included 41 healthy, premenopausal women age 18 to 55 who had taken OCs for at least three months, and were willing to switch to the study OC.

Participants received the combination OC for two or three 28-day cycles. Blood was collected during the second cycle (day 14) to measure EE and NOR levels. Administration of Zonegran began on day 15 of the second cycle, at 100 mg/d. The dose was increased by 100 mg every five days, to a target of 400 mg/d, given in evenly divided doses every 12 hours. Subjects were required to remain on their final daily dose for at least 12 days. EE and NOR levels were then measured in the third cycle (generally day 14, range 14-21 days) in the presence of Zonegran.

Thirty-seven subjects received Zonegran; two dropped out due to adverse events and two at their request. The researchers compared the concentrations of EE and NOR during OC dosing alone to those following the administration of Zonegran. Mean serum EE and NOR concentrations were similar before and after Zonegran dosing, indicating that steady-state dosing of Zonegran had no clinically relevant effect on the pharmacokinetics of EE or NOR.

Because this study was conducted in healthy individuals, the titration schedule was more aggressive than the schedule recommended for people with epilepsy. Despite rapid titration, Zonegran was reasonably well-tolerated in 26 subjects at the target dose of 400 mg/d when taken with a combination OC containing EE and NOR, although the incidence of AEs was somewhat higher than when dose escalation is slower. Treatment-emergent adverse events (AEs; occurring after administration of Zonegran) were reported in 33 of the 37 participants, and were primarily mild. The most frequently reported AEs were headache, nausea, weakness and dizziness. No death or serious AEs occurred.

### **Information about Zonegran**

Zonegran is an anti-epileptic drug approved in March 2000 by the FDA as adjunctive therapy in the treatment of partial seizures in adults with epilepsy.

Zonegran is a sulfonamide. Hypersensitivity or other serious reactions may occur. Serious skin and hematologic reactions (in the blood or blood-forming organs) have occurred. Physicians should consider discontinuing the drug in patients who develop an otherwise unexplained rash. Oligohidrosis (decreased sweating) has been reported in association with Zonegran therapy in pediatric patients. Zonegran is not approved for pediatric patients under the age of 16. Kidney stones have been reported in patients receiving Zonegran therapy. Patients should take special care when driving or if they operate complex machinery until they know how Zonegran may affect their performance. In clinical trials, the most commonly reported adverse events were somnolence, dizziness, anorexia, headache, nausea and agitation/irritability.

For more information about managing epilepsy and about Zonegran, and for full prescribing information for Zonegran, please visit [www.zonegran.com](http://www.zonegran.com). Please also see accompanying prescribing information.

Eisai acquired exclusive North American and European manufacturing and marketing rights to Zonegran from Elan in 2004. Elan had previously licensed Zonegran from Dainippon Pharmaceutical Co., Ltd. In Japan, the product is marketed by Dainippon under the brand name Excegran.

**About Eisai Inc.**

Eisai Inc. is a U.S. pharmaceutical subsidiary of Eisai Co., Ltd., a research-based *human health care (hhc)* company that discovers, develops and markets products in more than 30 countries. Established in 1995, Eisai Inc. began marketing its first product in the United States in 1997 and has rapidly grown to become an integrated pharmaceutical business with sales of more than \$1.7 billion (year ended March 31, 2004).

Eisai Inc. employs approximately 1,100 people at its headquarters in Teaneck, NJ, at its state-of-the-art pharmaceutical production and formulation research and development facility in Research Triangle Park, NC, and in the field. Between 1998 and 2003, Eisai Inc. moved up rapidly in the rankings (based on revenues) of U.S. pharmaceutical companies from No. 44 to No. 20.

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