News Alert from AdverseEvents, Inc.
UNDER EMBARGO UNTIL [September 27, 2011]
FDA AE Hotline (888) 463-6332

INDICATION OF INCREASED BIRTH DEFECT RISKS IN TWO FDA-APPROVED EPILEPSY MEDICATIONS MAY REQUIRE ACTION

AdverseEvents calls for FDA attention regarding current pregnancy category listings for both Lamictal and Keppra

HEALDSBURG, CA (September 27, 2011) – AdverseEvents, Inc. utilized RxFilter™, a proprietary data aggregation and refinement process, to determine that two epilepsy category C class drugs (defined by the U.S. Food and Drug Administration (FDA) as associated with "no known human risk") may be substantially more dangerous to a fetus than previously recognized. This analysis supports the reclassification of such medications as category D class drugs, defined by the FDA as associated with "positive evidence of human fetal risk". Given the FDA's central role in prescribing guidance, it is vital that pregnancy-related category warnings be updated in a timely and accurate manner. These new data revealed by the AdverseEvents' RxFilter process indicate that the FDA's current categorization of pregnancy-related risks may need immediate revision in order to mitigate fetal risks.

Healthcare providers rely almost exclusively on FDA "pregnancy category" warnings that are designed to highlight threats to a developing fetus. These categories are labeled class A ("no known risk"), B, C, D, and X ("DANGER - do not use") in order of decreasing benefit to risk ratio. While epilepsy drugs are acknowledged as a risk factor for congenital abnormalities, the magnitude of such risks has failed to be properly recognized. Epileptic women are especially at risk because most do not have the option of discontinuing their medication use during their pregnancies. AdverseEvents utilized their proprietary RxFilter system to perform a detailed analysis regarding links between anti-epilepsy medications and birth defects disclosed in the FDA's Adverse Event Reporting System (AERS).

Methodology
RxFilter, a proprietary 17-step data refinement process developed by AdverseEvents, was used to analyze the FDA's AERS database for treatment-related birth defects, stillbirths and congenital abnormalities potentially linked to 18 anti-epilepsy medications commonly prescribed during pregnancy. The time period of analysis was January 1, 2004 to March 31, 2011.

Results
Analysis with the RxFilter process indicated that two category C class epilepsy drugs (Lamictal and Keppra) might actually be as dangerous to a fetus as drugs currently listed in category D. In fact, an average birth defect rate comparison between top category C and D drugs yielded a surprising result; no meaningful differences were found between the two groups. Anti-epilepsy drugs that were examined included: Carbatrol/Tegretol, Depacon/Kene/Kote, Dilantin, Keppra (and IR), Klonopin, Lamictal, Neurontin, Topamax, Trileptal, and Zonegran. The use of RxFilter indicates that the FDA's current categorization of pregnancy risks may need revision.

Name of Drugs: Carbatrol/Tegretol, Depacon/Kene/Kote, Dilantin, Keppra (and IR), Klonopin, Lamictal, Neurontin, Topamax, Trileptal, and Zonegran

Main Treated Diseases: Epilepsy and related seizure disorders

Incidents/Adverse Events: Birth defects and stillbirths

Conclusion
Birth defects are an extremely serious adverse drug event associated with a range of prescription drugs. Epileptic women are especially at risk because most do not have the option of discontinuing their medication during pregnancy. About half of the

most widely prescribed epileptic medications are in category D, indicating a significant risk to a fetus. The other half are in category C, indicating less of a risk to the fetus than those in category D. Analysis using the RxFilter process, however, indicated that certain category C class drugs may actually be as dangerous to a fetus as drugs currently listed in category D. These results indicate that regulatory bodies may want to consider category shifts for some of the most widely used anti-epilepsy medications. Prospective studies, however, are needed to establish the exact incidence of these adverse events and to determine appropriate changes in category labeling, if any. This analysis warrants the attention of all healthcare providers and patients associated with epilepsy medications.

As is the case for any information in regards to side effects and adverse events, patients should never discontinue, or alter in any way, the drugs or dosages prescribed by their physician until after consultation with their doctor. Patients should discuss these findings directly with their doctors before making any changes whatsoever to their medicines or prescribed medication regimen.

About AdverseEvents, Inc.
AdverseEvents, Inc. (AEI) is the first service provider to deliver accurate, real-time information on adverse drug events reported to the FDA. AEI utilizes a unique data sourcing method called RxFilter™, a proprietary 17-step data refinement process that standardizes and normalizes the data from the FDA's Adverse Event Reporting System (AERS) into a user-friendly, fully searchable database of all FDA approved medications. Over 500,000 medication adverse events are reported yearly to the FDA; estimated to be only 10 percent of all actual adverse events. As a leading resource for the pharmaceutical industry, AEI supports companies with competitive intelligence and data to inform drug marketing decisions and business development strategies. With AEI, the healthcare industry is able to quantify the benefit-risk assessments of FDA approved drugs to fully understand the scope of safety issues, based on accurate rates of side effects from such medications. For more information about Adverse Events, please visit www.adverseevents.com.

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