



Neurology and Pharmacy Experts Reexamining Substitution of Antiepileptic Drugs

June 27, 2007 – STOCKTON, CA – A growing controversy over substituting generic antiepileptic drugs (AEDs) for their brand name counterparts will impact pharmacists, prescribers, and patients with epilepsy.

Almost all older anti-epilepsy drugs are already available generically. Many newer agents have recently gone generic, and nearly all epilepsy drugs will be available generically over the next few years. Generic substitution in pharmacies is common, legal, well accepted, and can save patients and insurers a lot of money.

Manufacturers of the newer anti-epilepsy drugs stand to lose a lot of money if generic equivalents are dispensed instead of the brand name medicines. Expect both insurance providers and drug manufacturers to try to sway practices to their benefit. The practice of switching to therapeutically equivalent generics could save more than \$20 billion a year. This figure represents revenue that the manufacturers don't want to lose and the insurance providers don't want to spend.

Critics of generic substitution for epilepsy drugs point out that epilepsy is different than other conditions. Many anti-epilepsy drugs must be used at very precise doses. Experts call this a "narrow therapeutic window." These narrow blood levels are required because slightly too little of the medicine may not control the patient's seizures, and slightly too much of the drug can lead to toxicity.

These critics point to potential variability among the many available generic products and say this increases the likelihood of a problem. For example, *Zonegran* went generic in 2005 and there are now over 15 different generic zonisamide products.

The FDA does allow a slight variability between generic and brand medications...and among generics... but this usually isn't a problem. Despite this, some experts worry that this small variability is too much in epilepsy, where the effectiveness of drugs is heavily dependent on consistency, and argue that generic substitution guidelines for anti-epilepsy drugs should be stricter than with other medications.

There are cases of drug toxicity or breakthrough seizures in patients switching to generic versions of older anti-epilepsy drugs like phenytoin (*Dilantin*), carbamazepine (*Tegretol*), and others. Breakthrough seizures can be devastating to epilepsy patients and may lead to loss of driving or work privileges. But most epilepsy experts say that similar equivalency problems aren't likely with generics of the newer meds because of different drug characteristics.

Most experts agree it is safe and economical to switch to a generic version of a drug when it is therapeutically equivalent. Any variability allowed by the FDA is very small and highly unlikely to impact a patient's therapy. Many states refer to the FDA's Orange Book rating for bioequivalence and authorize substituting "A-rated" drugs. Experts say generic substitution can save money for patients and provides equal therapeutic effects when bioequivalent and therapeutically equivalent products are substituted.

“The key for health professionals is to focus on the needs of the patient.” says Kristin Weitzel, PharmD, CDE, Assistant Editor for *Pharmacist’s Letter*. “Pharmacists are in an ideal position to help epilepsy patients by using their clinical judgment and following their state’s substitution laws for epilepsy drugs. For example, there are many AB-rated generics for phenytoin, but it’s probably a good idea to keep phenytoin patients on the same product if you can from refill to refill. This can help to decrease any potential variability among epilepsy patients that may have problems. Keep in mind you don’t necessarily need to do this with every epilepsy medication, but it may help some patients on older agents like phenytoin and carbamazepine.”

Experts at *Pharmacist’s Letter* indicate that many of the anti-seizure drugs are used for many purposes other than treating epilepsy. In these instances, the slight variations in the drug products are even less likely to be noticed in a patient. If a blanket requirement to avoid therapeutic substitution were to apply to all anti-seizure drugs, many patients without seizure problems would pay significantly higher prices for products that offered no increase in benefit.

Pharmacist’s Letter provides health professionals with a thorough analysis of these issues at www.pharmacistsletter.com/newsroom/aeds. There, they can read both concise recommendations and the *Pharmacist’s Letter Detail-Document* that explores the issue in greater depth.

Pharmacist’s Letter also provides a chart that details the current laws governing the substitution of generic drugs on a state by state basis and provides FDA Orange Book ratings for all generically available epilepsy medications. It can be found at www.pharmacistsletter.com/newsroom/generic.

About *Pharmacist’s Letter* and Therapeutic Research Center

Pharmacist’s Letter is a subscription service that provides recommendations for pharmacists on new developments in drug therapy, and trends in pharmacy practice. *Pharmacist’s Letter* started in 1985 and currently serves most pharmacists in the United States and Canada. The service consists of a monthly letter, plus *Detail-Documents* available 24 hours a day.

Therapeutic Research is a completely independent research and publishing organization that provides evidence-based information for physicians, pharmacists, and other medical professionals. In addition to *Pharmacist’s Letter*, Therapeutic Research publishes *Prescriber’s Letter*, a similarly formatted advisory service for prescribers, as well as *Natural Medicines Comprehensive Database*, *Ident-A-Drug Reference*, and a variety of continuing medical education courses including live courses. Therapeutic Research accepts no advertising and provides objective information for subscribers.

Contact

Greg Tripp
Web Editor
Therapeutic Research Center
Therapeutic Research Faculty
3120 West March Lane
Stockton, CA 95219
Phone: 209-472-2240
Fax: 209-472-2247
<http://www.pharmacistsletter.com/newsroom>
greg.tripp@pletter.com

###