Variation in make-up of generic epilepsy drugs can lead to dosing problems

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Generic anti-epilepsy drugs, pharmaceutical products similar to brand-name versions, save consumers billions of dollars each year, but some are different enough from branded formulations that they may not be effective, particularly if patients switch between two generic drugs, a new study by Johns Hopkins researchers suggests. A report on the study, published online and in an upcoming issue of *Annals of Neurology*, raises questions about whether some generic products are safe and effective when a narrow dose range separates patients from help and harm.

“In most areas of medicine, generics work well and are an incredible savings for health plans and patients,” explains study leader Gregory Krauss, M.D., professor of neurology at the Johns Hopkins University School of Medicine. However, he adds, epilepsy patients whose condition is well-controlled on brand-name medications often worry that switching to generic versions might change blood medication levels, leading to seizures and side effects. These fears aren’t without merit — studies have shown that patients frequently complain of breakthrough seizures when switched to generic drugs.

Consequently, Krauss and his colleagues decided to compare how generics stack up to their brand-name counterparts, as well as other generic formulations for the same drug, using the bioequivalence study data that generic manufacturers generate to gain U.S. Food and Drug Administration (FDA) approval. Such data, held privately by the FDA, are mandated by the Drug Price Competition and Patent Term

Restoration Act (informally known as the Hatch-Waxman Act). Part of this law, passed during the Reagan administration, states that generic formulations must have a peak blood concentration and total amount absorbed that falls between 80 percent and 125 percent of the name-brand version.

That range is suitable for the vast majority of pharmaceuticals, says Krauss. However, he notes, for some "critical dose" drugs that have a high potential for over- or underdosing, the window could be significantly narrower.

After securing bioequivalency data for 141 generic epilepsy drugs from the FDA using Freedom of Information Act requests, Krauss and his colleagues found that peak blood concentration and total amount absorbed differed by less than 15 percent between the vast majority of generics and their brand-name equivalents. However, some manufacturers had generic products that were at the upper or lower edge of the acceptance limits, and these drugs varied markedly between each other compared to the brand-name drugs—as much as 30 percent between generic formulations for one drug in particular, oxycarbazepine.

Since each brand-name drug can have many different generic counterparts — and pharmacies frequently switch between different generic versions — prescriptions for some generic drugs could prove unsafe for epilepsy patients, Krauss notes.

"Overall, generics should be used for treating epilepsy," Krauss says. "However, we suggest that patients and pharmacies should be cautious when switching between different generic version of anticonvulsants, and policy makers should evaluate whether standards that set the range for generics' similarity to brand name versions are appropriate for every drug. For patients with epilepsy, that may not be the case."

He notes that for other pharmaceuticals in which over- or underdosing by narrow margins may also be a problem, such as chemotherapeutics for cancer, the same questions can be raised.

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