Study of generic antiepilepsy drugs finds minimal differences

December 10 2014, by Keith Herrell

A comparison of two of the most disparate approved generic antiepileptic drugs found minimal differences when compared under rigorous testing procedures in people with epilepsy, according to research presented by a University of Cincinnati (UC) clinician-researcher.

In addition, the research showed, no subjects had serious adverse effects or loss of seizure control when switching from one drug to the other.

Michael Privitera, MD, a professor in the UC Department of Neurology and Rehabilitation Medicine and director of the Epilepsy Center at the UC Neuroscience Institute, presented the research Saturday, Dec. 6, at the annual meeting of the American Epilepsy Society in Seattle.

Privitera and colleagues at UC, the University of Rochester and four other centers received $2.6 million from the U.S. Food and Drug Administration in 2013 to study generic equivalents for the U.S. Food and Drug Administration-approved antiepileptic drug lamotrigine (marketed by GlaxoSmithKline as Lamictal), as part of an effort to provide the FDA with data that could lead to new regulations related to approval of new generic drugs. The American Epilepsy Society and the Epilepsy Foundation also contributed to the study. (Privitera reports no conflicts of interest.)

The study, along with a separate effort comparing two generic copies with Lamictal, is known as EQUIGEN, or EQUIvalence among GENeric

AEDS (antiepileptic drugs).

"Some physicians and patients perceive that generic antiepileptic drugs are not always equivalent to brand products," says Privitera, who noted that the FDA currently approves generic drugs by requiring studies on normal volunteers (i.e., those who don't have epilepsy) and who take just one dose of the generic drug followed by a series of blood tests.

"We designed this study to address those concerns and mimic real-life circumstances for epilepsy patients."

Several studies of thousands of patients have suggested that hospitalizations and doctor visits are more common in people with epilepsy after switching to generic drugs. However, these studies did not carefully measure blood levels or control for other factors. The EQUIGEN studies were designed to control for missed doses and rigorously measure blood levels, obtaining blood levels over 12 hours.

To meet FDA standards, generic versions of a brand name drug must have 80 percent to 125 percent bioequivalence of the original drug. Privitera and his colleagues tested two generics that had achieved that standard in single-dose studies with normal volunteers: one generic on the low end, and one on the high end.

"That way, we were testing the worst-case scenario," Privitera says: "That the patient could go to a pharmacy and get the generic product at the high end of the bioequivalency scale, then go back the next time and get the product on the low end of the scale."

The researchers divided study participants (33 out of 35 original participants completed the study) into two groups, with each group switching generic copies twice over four test periods. Patients also continued their usual medications, including antiepilepsy drugs. At the

end of each two-week test period, the participants underwent extensive blood level monitoring.

"None of the subjects had any serious adverse events or loss of seizure control after crossover between generic products," Privitera reports, adding that the results showed that chronic dosing studies are feasible and that subjects are highly compliant. (There were no dropouts due to lack of compliance.)

In the other EQUIGEN study, researchers are comparing the two generic copies with Lamictal, the brand-name version of lamotrigine. Participants take each medicine twice during the study period. This is a "single dose" study, in which patients take a single dose of generic lamotrigine in addition to their regular antiepileptic drugs and then have rigorous blood level testing over a 96-hour period.

Results of that study are expected in early 2015.

Provided by University of Cincinnati