The Examiner

Opinion

Drug cost reduction can’t compromise patient safety

By Daniel J. Popeo
Examiner Contributor | 3/22/09 4:55 PM

Generic drugs, which were burdened by doubt and scandal just two decades ago, now account for 65 percent of U.S. prescriptions and are a centerpiece of President Barak Obama’s plan to reduce what he calls “the exploding costs of health care in America.”

Consumers’ continued high confidence in generics, and in large part the success of drug cost containment, relies upon the Food and Drug Administration’s (FDA) assurance that such treatments are safe.

FDA’s review of generic drugs has received little attention when compared to the agency’s oversight of branded drugs. But now that these copycat drugs play a leading role on the national health care stage, it’s time to shine a brighter light on their approval. This heightened attention should focus on past missteps and troubling policies which, if not addressed, can compromise patient safety.

Generics do not undergo the same rigorous testing as the innovative drugs they copy. Rather, as an effective surrogate for proof of safety and efficacy, FDA must find that the generic is identical or *bioequivalent* to the original drug in dosage, form, strength, and rate and route of absorption.

The rate and route of absorption in the body, for instance, is especially critical for “controlled-release” medicines. Such drugs provide patients with specific drug doses at precise time intervals, which is highly effective for those suffering from conditions such as Alzheimer’s, Parkinson’s, and depression.

Unfortunately, FDA uses outdated bioequivalence standards that do not accurately account for the sophisticated time sequencing of controlled-release products. With over 20 applications for copies of controlled-release drugs pending at FDA, the agency's failure to update its testing approach could negatively impact millions of Americans who might be switched to an inexact generic.

The case of one particular generic antidepressant reflects the potential consequences of approving copies with inexact controlled-release technology. This controlled-release antidepressant was available in 150 and 300 milligram strengths. FDA's 2006 approval of the generic antidepressant allowed copies to be made of both versions of the drug even though the agency only tested bioequivalence of the 150 mg product.

Soon after approval, numerous patients who had been switched to the generic complained that their depression had returned, with some attempting suicide. Independent tests of the 300 mg version revealed that 34% of the generic dissolved after two hours, compared to 8% in the branded drug.

FDA reviewed the generic's bioequivalence in late 2007, and six months later restated its original conclusion that the generic and branded were identical. Consumer complaints continued, and last September FDA finally began contemplating further study of the 300 mg version of the generic antidepressant.

Other instances where FDA has made questionable judgments involving generics of complex drugs have arisen over the past several years. Last April, FDA approved a generic version of a topical cream for treating both pre-cancerous skin growths and deeply encased skin cell carcinoma, even though bioequivalence was proven only for the less serious growths.

The manufacturer of a pill to treat life-threatening gastrointestinal infections, along with numerous clinicians and doctors, has vigorously opposed FDA's effort to simplify the approval process of a generic version of the drug. With no public input or notice, generic reviewers replaced the long-standing practice of requiring human clinical trials for such locally-acting drugs with cheaper and quicker test tube examination.

Federal law justifiably provides FDA with flexibility in how it determines bioequivalence for generics. But that discretion should not be used to favor speed to market over patient safety. Doing so could severely undermine policymakers' plans to reduce drug costs.

Dissimilar generics which cause harm or are ineffective could necessitate further, more costly health services, such as hospitalization. Such products could expose generic manufacturers to litigation and, thanks to a bizarre California court ruling, also places the original branded drug's manufacturer in legal peril. Litigation, and the concomitant damage to reputation it inflicts, directly increases drug costs and indirectly frustrates new drug development. And instances of harm or ineffectiveness will undercut consumers' confidence in the equivalence of generic drugs.

Obama’s incoming health care team has an opportunity to inject consistency, transparency, and sounder science into the generic drug review process. FDA’s recent decision to review generic bioequivalence standards is a very encouraging step in the right direction.

As medical technology expands, treatments will become increasingly complex, and Congress and the administration must ensure that patient safety is not sacrificed in a worthy drive to reduce health costs. Getting it right on issues such as generic bioequivalence today will benefit Americans for generations to come.

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