Understanding Generics

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As dermatologists, we are lucky to be in a specialty in which we can take care of our patients with mostly topical treatments, avoiding possible systemic adverse events that can accompany oral medications. On the other hand, the importance of vehicles that deliver the topical treatments to the skin is unfortunately underrated and misunderstood, mostly by non-dermatologists; the generic substitution of most of our prescriptions by pharmacists being the best proof of this misunderstanding. Unfortunately, the daily generic substitution of our prescriptions has become routine, and it is here to stay as the pressure for cost-saving efforts in medicine increases with the new health care environment.

Let's take a brief look at the generic approval process for oral drugs in the United States. A generic drug aims to match the branded product in terms of active ingredient and dosage form by bioequivalence to the Reference Listed Drug or Innovator (Branded Drug). Oral generic drugs have to show equivalent bioavailability through comparable plasma concentrations. This process for oral medications is as simple as it seems.

Now, let's take a detailed look at the generic approval process for topical drugs in the United States. The methods of demonstrating bioequivalence are more complicated for topicals than for oral medications because plasma concentrations are really not a good measure.

There are 3 different ways for a generic topical drug to meet the bioavailability criteria:

1. Bioequivalence waiver from the US Food and Drug Administration

2. Clinical bioequivalence for all non-corticosteroid topical drugs in a 3-arm study in which the generic product is tested against the reference drug and the vehicle

3. Bioequivalence by a vasoconstriction bioassay for all topical corticosteroid generics. This bioassay, known as the Stoughton and McKenzie Assay, measures the area under the effect curve which is related to the potency of that particular corticosteroid. The test is performed on the volar forearm of healthy volunteers by measuring the blanching effect of the generic topical corticosteroid over an established period of time with a chromameter.

The bioequivalence requires that the test product (generic) does not differ "significantly" from the reference product (innovator). This significance is defined as 20%. That translates to a 45% variability, which means one generic can vary by 45% from the innovator or from another generic.[1]

This generic approval process for topical corticosteroids, which are the most commonly used drugs in dermatology, poses several challenges: Our patients can receive a different generic each time they fill their prescription. It is not unusual for patients to tell us, "That salve was working really well, but it is just not working anymore." We immediately think about tachyphylaxis or non-adherence, but perhaps it is just that they received a generic this month with 45% less bioequivalence than the generic they received last month! Perhaps they received a generic that has an excipient in the vehicle to which they are allergic. Perhaps they received a generic that has no clinical efficacy, since vasoconstriction assay does not test for clinical efficacy at all and is performed on healthy skin. Perhaps they received a generic with a vehicle that just rubs off the skin without penetrating the stratum corneum at all. Perhaps they received a generic that needs to be dosed 3 times a day rather than twice a day, since vasoconstriction assay is a single application test. Or perhaps they received a generic with a vehicle full of irritants that impairs the epidermal barrier and increases

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transepidermal water loss, since vasoconstriction assay does not test application site reactions. For all of these reasons, I am worried about my patients' well-being every time I write a generic topical corticosteroid prescription.

However, we now have branded generics in which the manufacturers have begun producing their own authorized generics with the exact same excipients as in their original branded vehicles. Promius Pharma, one of the leaders in this field, recently brought to the market clocortolone pivalate 0.1% generic formulation, which is exactly the same as their original branded product. Another advantage is that this formulation is the only authorized generic formulation of clocortolone pivalate 0.1% cream on the market.[2]

The new trend of authorized exact same generics of unique products such as clocortolone pivalate 0.1% is a welcome addition to our treatment armamentarium and a great service to our patients, allowing me to prescribe this generic formulation without any of the above concerns.

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Disclosures

Dr. Kircik has received compensation from the *Journal of Drugs in Dermatology* for his editorial support.

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