

## **Draft Guidance on Betamethasone Valerate**

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind the FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

**Active Ingredient:** Betamethasone valerate

**Dosage Form; Route:** Foam aerosol; topical

**Recommended Studies:** Two options: waiver or in vivo

### **I. Waiver Option**

- a. To qualify for a waiver of the in vivo bioequivalence (BE) study requirements under 21 CFR 320.22(b)(3), a generic betamethasone valerate foam aerosol/topical, 0.12% must be a solution for aerosolization; have the same active ingredient in the same concentration and dosage form as the reference listed drug product (RLD); and must not have an inactive ingredient or other change in formulation from the RLD that may significantly affect systemic or local availability.
- b. For a topical drug product with inactive ingredients that differ from the RLD or are present in significantly different amounts [as permitted by the chemistry, manufacturing, and controls regulations for abbreviated new drug applications (ANDAs), 21 CFR 314.94(a)(9)(v)], the regulation specifies that the applicant must identify and characterize the differences and provide information demonstrating that the differences do not affect the safety or efficacy of the proposed drug product. If the generic betamethasone valerate foam aerosol/topical, 0.12% has different inactive ingredients compared to the RLD or differences in the amounts of the same inactive ingredients that are proportionally more than +/- 5% compared to the RLD, then the Office of Generic Drugs (OGD) may request a bioequivalence study with clinical endpoints to determine bioequivalence between the products.
- c. For products applied to the scalp, differences in surfactants or potential penetration enhancers may change the distribution of the product over the scalp or penetration of the drug into the diseased tissues. Therefore, clinical endpoint bioequivalence studies are requested for generic shampoo products with differences in these ingredients that are proportionally more than +/- 5% compared to the RLD.
- d. To support the waiver request, data from the following comparative in vitro assays of test vs. reference are requested:
  - Microscopic Birefringence Analysis on the dispensed Aerosol, Foam after complete collapse to determine whether any crystals of undissolved betamethasone valerate form during dispensing.

- Time to Break Analysis, conducted at 30°C, 33°C, 35°C, and 40°C. Time to break is the time from dispensing to complete Aerosol, Foam collapse (break). The testing should be done on at least 3 different lots of the RLD and at least 3 lots of the test product (with each lot manufactured separately).
  - Weight per volume of uncollapsed aerosol, foam.
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## **II. In Vivo Option:**

Recommended studies: 1 study

Type of study: Clinical endpoint bioequivalence (BE) study

Design: Randomized, double-blind, parallel, placebo-controlled in vivo

Strength: 0.12%

Subjects: Healthy males and females with moderate to severe corticosteroid-responsive scalp psoriasis

Additional comments: FDA recommends submitting a protocol for review and comment prior to conducting the study.

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**Analytes to measure (in appropriate biological fluid):** Not applicable (N/A)

**Bioequivalence based on (90% CI):** Clinical endpoint (in vivo option)

**Dissolution test method and sampling times:** N/A