Contains Nonbinding Recommendations

Draft Guidance on Clindamycin Phosphate

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

Active Ingredient: Clindamycin phosphate

Dosage Form; Route: Aerosol, foam; topical

Recommended Studies: Two options: (1) waiver or (2) an in vivo study with clinical endpoint

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1. Option 1: Waiver

A. To qualify for a waiver of the in vivo bioequivalence study requirement under 21 CFR 320.22(b)(3), generic versions of clindamycin phosphate topical aerosol foam, 1% should contain the same active ingredient in the same concentration and dosage form as the reference product and contain no difference in inactive ingredients or in other aspects of the formulation relative to the reference product that may significantly affect the local or systemic availability of the active ingredient. A proposed clindamycin phosphate topical aerosol foam should contain an amount of clindamycin phosphate equivalent to 1% of clindamycin free base in order to be considered the same strength as, and pharmaceutically equivalent to, the reference product.

B. For a topical solution drug product that differs from the reference product in inactive ingredients [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.

C. To support the waiver request, data from the following comparative in vitro assays of the test and reference products is requested:

   i. Microscopic birefringence analysis on the dispensed foam after complete collapse to determine whether any crystals of undissolved clindamycin phosphate form during dispensing.

   ii. 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 foam collapse (break). The testing should be done on a minimum of three batches of the test and three batches (as available) of the reference product.

iii. Weight per volume of uncollapsed foam.

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2. Option 2: In vivo study with clinical endpoint

Type of study: Bioequivalence study with clinical endpoint
Design: Randomized, double blind, parallel, placebo-controlled, in vivo
Strength: 1%
Subjects: Males and nonpregnant, nonlactating females with acne vulgaris
Additional comments: Applicants intending to utilize the in vivo option to demonstrate bioequivalence should refer to the guidance for industry *Controlled Correspondence Related to Generic Drug Development* and the guidance for industry *Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA* for additional information describing the procedures on how to clarify regulatory expectations regarding your individual drug development program.

Analytes to measure (in appropriate biological fluid): Not applicable

Bioequivalence based on (90% CI): Clinical endpoint

Dissolution test method and sampling times: Not applicable