

Draft Guidance on Diclofenac Sodium

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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: Diclofenac Sodium

Form/Route: Solution/Topical

I. Waiver option:

- a. To qualify for a waiver of the in vivo bioequivalence study requirement under 21 CFR 320.22(b)(3), generic versions of Diclofenac Sodium Topical Solution, 1.5% must contain the same active drug ingredient in the same concentration and dosage form as the Reference Listed Drug (RLD) and contain no inactive ingredient or other change in formulation from the RLD that may significantly affect systemic or local availability of the active ingredient.
- b. For a topical drug product that differs from the RLD in inactive ingredients [as permitted by the chemistry, manufacturing and controls regulations for abbreviated new drug applications, 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 version of Diclofenac Sodium Topical Solution, 1.5% 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 and/or a bioequivalence study with pharmacokinetic endpoints and/or a skin irritation and sensitization study to determine bioequivalence between the products, especially if the differences involve potential penetration enhancers.

II. In Vivo option:

Recommended studies: 2 studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover in vivo
Strength: 1.5%
Subjects: Healthy males and non-pregnant females, general population.
Additional comments: None
2. Type of study: Bioequivalence (BE) Study with Clinical Endpoint
Design: Randomized, double blind, parallel, placebo-controlled in vivo
Strength: 1.5%
Subjects: Healthy males and females with osteoarthritis of the knee.
Additional comments: FDA recommends submitting a protocol for review and comment prior to conducting the study.

Analytes to measure (in appropriate biological fluid): Diclofenac in plasma (in vivo option, Study 1)

Bioequivalence based on (90% CI): Diclofenac in plasma (in vivo option, Study 1); Clinical endpoint (in vivo option, Study 2)

Waiver request of in vivo testing: Not Applicable

Dissolution test method and sampling times: Not Applicable