

Draft Guidance on Diclofenac Sodium

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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: Diclofenac sodium

Dosage Form; Route: Solution; topical

I. Waiver option:

- a. A waiver of the in vivo bioequivalence studies may be requested if generic versions of Diclofenac sodium topical solution, 2% 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 bioavailability of the active ingredient.
- b. For a topical drug product that differs from the RLD in inactive ingredients, the applicant should 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, 2% 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 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: Two studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover in vivo
Strength: 2%
Subjects: Males and non-pregnant, non-lactating females, general population.
Additional comments: Ensure adequate washout periods between treatments in the crossover studies due to diclofenac's long terminal elimination half-life. Consider using a parallel study design. Collect sufficient blood samples in the bioequivalence studies to adequately characterize the peak concentration (C_{max}) and time to reach peak concentration (T_{max}).

2. Type of study: Bioequivalence (BE) Study with Clinical Endpoint
Design: Randomized, double blind, parallel, placebo-controlled in vivo
Strength: 2%
Subjects: Patients with osteoarthritis of the knee, including males and non-pregnant, non-lactating females.
Additional comments: None
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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