Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Methoxsalen

October 2024

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

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Active Ingredient: Methoxsalen

Dosage Form: Capsule

Route: Oral

Strength: 10 mg

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 10 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments:
   a. It is permissible to administer more than one capsule for the study to obtain adequate plasma concentration of the analyte to be measured.
   b. Exclude subjects with photosensitivity.
   c. Do not allow subjects to be in sunlight (direct or indirect, even through window glass or cloud cover) for 8 hours post dose and subjects should be required to wear UVA-absorbing, wrap-around sunglasses during the daylight hours for the 24-hour period post dose. Participants should appropriately be advised of these restrictions in the informed consent.
   d. Applicants may consider using a reference-scaled average bioequivalence approach. If using this approach, provide evidence of high variability in the pharmacokinetic parameters (i.e., within-subject variability ≥30%) for the reference listed drug (RLD). For detailed information on this approach, refer to the most recent version of the FDA guidance for industry on *Bioequivalence Studies with Pharmacokinetic Endpoints for Drugs Submitted Under an ANDA.*[a]

Analyte to measure: Methoxsalen in plasma

Waiver request of in vivo testing: Not applicable

Dissolution test method and sampling times: The dissolution information for this drug product can be found in the FDA's Dissolution Methods database, http://www.accessdata.fda.gov/scripts/cder/dissolution/. Conduct comparative dissolution testing on 12 dosage units for each of the test product and RLD.[1] Specifications will be determined upon review of the abbreviated new drug application.

Document History: Recommended April 2010; Revised October 2024

Unique Agency Identifier: PSG_009048

[a] For the most recent version of a guidance, check the FDA guidance website at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[1] If the RLD is not available, refer to the most recent version of the FDA guidance for industry on *Referencing Approved Drug Products in ANDA Submissions*.