

Contains Nonbinding Recommendations
Draft Guidance on Methoxsalen

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Capsules/Oral

Recommended studies: 2 studies

1. Type of study: Fasting

Design: Single-dose, two-way crossover *in-vivo*

Strength: 10 mg

Subjects: Healthy males and nonpregnant females, general population.

Additional Comments:

- To avoid or minimize the GI side effects, doses should be administered with 240 mL of low-fat milk
- It is permissible to administer more than one capsule for the study to obtain adequate plasma concentration of the analyte to be measured.
- Please exclude subjects who receive concomitant therapy (topically or systemically) with known photosensitizing agents.
- Please 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.
- Applicants may consider using a reference-scaled average bioequivalence approach for this highly variable drug substance/product. Provide evidence of high variability in the bioequivalence parameters, AUC and/or C_{max} (i.e., within-subject variability $\geq 30\%$) when using this approach. For general information on this approach, please refer to Haidar et al., Bioequivalence Approaches for Highly Variable Drugs and Drug Products, Pharm. Res. 25:237-241(2008).

2. Type of study: Fed

Design: Single-dose, two-way crossover *in-vivo*

Strength: 10 mg

Subjects: Healthy males and nonpregnant females, general population.

Additional Comments: Doses should be administered with 240 mL of water. Please see additional comments above.

Analytes to measure (in appropriate biological fluid): Methoxsalen in plasma

Bioequivalence based on (90% CI): Methoxsalen

Waiver request of in-vivo testing: Not Applicable

Dissolution test method and sampling times: Please note that a **Dissolution Methods Database** is available to the public at the OGD website at <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. Please find the dissolution information for this product at this website. Please conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products. Specifications will be determined upon review of the application.