Contains Nonbinding Recommendations

Draft Guidance on Acitretin

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Capsules/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
   Design: single-dose, two-way crossover *in-vivo*
   Strength: 25 mg
   Subjects: Normal healthy males and females, general population.
   Additional Comments: Pregnant female subjects should be excluded from the bioequivalence studies.

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2. Type of study: Fed
   Design: single-dose, two-way crossover *in-vivo*
   Strength: 25 mg
   Subjects: Normal healthy males and females, general population.
   Additional comments: Please see comment above.

Analytes to measure: All-trans-acitretin and 13-*cis*-acitretin in plasma

Since acitretin undergoes extensive presystemic metabolism and interconversion by isomerization to 13-cis-acitretin, measurement of all-trans-acitretin and 13-cis-acitretin in plasma is recommended. The pharmacokinetic parameters for all-trans-acitretin should meet the current bioequivalence criteria. The 13-cis-acitretin data will be used as supportive evidence. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and Cmax.

Bioequivalence based on (90% CI): All-trans-acitretin

Waiver request of in-vivo testing: 10 mg based on (i) acceptable bioequivalence studies on the 25 mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

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.fda.gov/cder/ogd/index.htm. 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.