

Draft Guidance on Chenodiol

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 250 mg
Subjects: Males and females of non-childbearing potential, general population
Additional comments: Consider using a parallel study design due to chenodiol's long half-life. For long half-life drug products with low intra-subject variability in distribution and clearance, an area under the concentration time curve (AUC) truncated to 72 hours may be used in place of AUC_{0-t} or $AUC_{0-\infty}$. For either a crossover or parallel study, sample collection time should be adequate to ensure completion of gastrointestinal transit of the drug product and absorption of the drug substance. Collect sufficient blood samples in the bioequivalence studies to adequately characterize peak concentration (C_{max}) and time to reach C_{max} .

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 250 mg
Subjects: Males and females of non-childbearing potential, general population
Additional comments: See comments above

Analyte to measure (in appropriate biological fluid): Chenodiol in plasma

Chenodiol is an endogenous substance. , For both fasting and fed studies, plasma concentrations of chenodiol should be corrected for baseline endogenous concentrations. This can be done by subtracting the mean value of several pre-dose measurements from each subsequent chenodiol concentration obtained after dosing. Any negative values, obtained from baseline correction, should be designated as zero (0) and any subject with baseline-corrected pre-dose concentrations (at time 0 hour) more than 5% of their C_{max} should be excluded from the bioequivalence statistical analysis and the 90% confidence intervals based on the remaining subjects. Baseline concentrations should be determined for each dosing period and baseline corrections should be period specific.

Bioequivalence based on (90% CI): Baseline-corrected chenodiol

Waiver request of in vivo testing: Not applicable

Dissolution test method and sampling times: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods web site, available to the public at the following location: <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. 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 abbreviated new drug application.