Contains Nonbinding Recommendations

Draft Guidance on Succimer

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Capsule; Oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 100 mg
   Subjects: Males, and non-pregnant and non-lactating females, general population
   Additional comments: Ensure adequate washout periods between treatments in the crossover studies due to its long terminal elimination half-life. A parallel study design may also be used due to the drug's long half-life. For long half-life drug products with low intra-subject variability in distribution and clearance, an AUC truncated to 72 hours may be used in place of AUC_{0-t} or $AUC_{0-\infty}$. For either a crossover or a 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 the peak concentration (Cmax) and time to reach peak concentration (Tmax).

---

2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 100 mg
   Subjects: Males, and non-pregnant and non-lactating females, general population
   Additional comments: See comments above

Analytes to measure (in appropriate biological fluid): Total succimer (meso-2,3-dimercaptosuccinic acid (DMSA)) including unaltered and altered in plasma

Bioequivalence based on (90% CI): Total DMSA

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 (ANDA).