Contains Nonbinding Recommendations

Draft Guidance on Lomitapide Mesylate

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Capsule; oral

Recommended Studies: One study

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in vivo
   Strength: EQ 60 mg Base
   Subjects: Healthy males, general population; females may be enrolled only if not of childbearing potential (see additional comments below)
   Additional comments:
   - Measurement of transaminase (ALT, AST), alkaline phosphatase, and total bilirubin should be performed before enrollment to ensure proper liver function
   - Due to the potential risk of fetal toxicity, women of reproductive potential enrolled in the study should meet one of the following requirements: (1) post-menopausal (2) surgically sterile
   - Exclude any subject who has taken a CYP 3A4 inhibitor (e.g., SSRIs, antifungals, antibiotics, oral contraceptives) within 4 weeks prior to enrollment; prohibit the concomitant use of any CYP 3A4 inhibitor during the study
   - Omit grapefruit juice from the diet while being dosed with lomitapide

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

Bioequivalence based on (90% CI): Lomitapide

Waiver request of in vivo testing: The 5, 10, 20, 30, and 40 mg strengths of lomitapide capsules are eligible for a waiver of in vivo bioequivalence (BE) testing provided that the following criteria are met: (i) the in vivo BE study on the 60 mg strength is acceptable; (ii) dissolution testing is acceptable; and (iii) the formulation of the 5, 10, 20, 30, and 40 mg strengths are proportionally similar to that of the 60 mg strength

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. Specification(s) will be determined upon review of the abbreviated new drug application (ANDA).