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Draft Guidance on Mavacamten

August 2023

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Active Ingredient: Mavacamten

Dosage Form: Capsule

Route: Oral

Strengths: 2.5 mg, 5 mg, 10 mg, 15 mg

Recommended Studies: Two in vivo bioequivalence studies with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 5 mg
   Subjects: Healthy males and females not of reproductive potential
   Additional comments: Exclude subjects with left ventricular ejection fraction <55%. Exclude CYP2C19 poor metabolizers. Mavacamten capsule is approved under a Risk Evaluation and Mitigation Strategy (REMS) with Elements to Assure Safe Use (ETASU), which restricts its use. All pertinent elements of the REMS/ETASU must be incorporated into the protocol and informed consent. Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of mavacamten. Alternatively, a parallel study design may be considered.

2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 5 mg
   Subjects: Healthy males and females not of reproductive potential
   Additional comments: See comments above.

Analyte to measure: Mavacamten in plasma

Bioequivalence based on (90% CI): Mavacamten

Waiver request of in vivo testing: 2.5 mg, 10 mg and 15 mg strengths based on (i) acceptable bioequivalence studies on the 5 mg strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths

Dissolution test method and sampling times: The dissolution information for this drug product can be found in the FDA's Dissolution Methods database, 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.

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