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Draft Guidance on Tivozanib Hydrochloride

November 2022

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Active Ingredient: Tivozanib hydrochloride

Dosage Form; Route: Capsule; oral

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: EQ 1.34 mg Base
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: Exclude subjects who have undergone or plan to undergo any surgery or dental procedure for at least two weeks prior to the study and at least 24 days after the study. Female subjects of reproductive potential should use non-hormonal contraception during the study and continue to use effective contraception for one month after the study. Male subjects with female partners of reproductive potential should use effective contraception during the study and for one month after the study. Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of tivozanib. Alternatively, a parallel study design may be considered.

2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: EQ 1.34 mg Base
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: See comments above.

Analyte to measure: Tivozanib in serum

Bioequivalence based on (90% CI): Tivozanib

Waiver request of in vivo testing: EQ 0.89 mg Base strength based on (i) acceptable bioequivalence studies on the EQ 1.34 mg Base strength, (ii) acceptable in vitro dissolution testing of both strengths, and (iii) proportional similarity of the formulations between both 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 for each of both strengths of the test and reference products. Specifications will be determined upon review of the Abbreviated New Drug Application (ANDA).

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