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Draft Guidance on Brexpiprazole

October 2024

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Active Ingredient: Brexpiprazole

Dosage Form: Tablet

Route: Oral

Strengths: 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-way, two-period crossover or parallel design in vivo
   Strength: 2 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: (1) Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of brexpiprazole. Alternatively, a parallel study design may be considered. (2) Dystonia has been reported among healthy subjects who received brexpiprazole tablets. To avoid potential risk of dystonia, subjects who are younger than 45 years or have a history of dystonia should be excluded. Adverse events associated with brexpiprazole appear comparable to those associated with the atypical antipsychotic class of drugs (i.e., aripiprazole). All the safety precautions for healthy volunteer studies of brexpiprazole are the same as those recommended for healthy volunteer studies of aripiprazole. Refer to the product specific guidance on aripiprazole tablets.

Analyte to measure: Brexpiprazole in plasma

Bioequivalence based on (90% CI): Brexpiprazole

Waiver request of in vivo testing: 0.25 mg, 0.5 mg, 1 mg, 3 mg, and 4 mg strengths based on (i) acceptable bioequivalence stud**y** on the 2 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 for each of all strengths of the test product and reference listed drug (RLD).[1] Specifications will be determined upon review of the abbreviated new drug application.

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[1] If the RLD is not available, refer to the most recent version of the FDA guidance for industry on *Referencing Approved Drug Products in ANDA Submissions.*