

Draft Guidance on Cariprazine Hydrochloride

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Capsule; oral

Recommended Studies: Two studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover in vivo
Strength: EQ1.5 mg Base
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comments: Ensure that there are adequate washout periods between treatments in the crossover study due to cariprazine's long terminal elimination half-life. Consider using a parallel study design due to its long half-life. For either a crossover or parallel study, sample collection time should be adequate to ensure completion of gastrointestinal transit of the drug product and absorption of the drug substance (which usually occurs within approximately 2 to 3 days). Use C_{max} and a suitably truncated AUC to characterize peak and total drug exposure, respectively. For drugs that demonstrate low intrasubject variability in distribution and clearance, use an AUC truncated at 72 hours ($AUC_{0-72\text{ hr}}$) in place of AUC_{0-t} or AUC_{0-inf} . For drugs demonstrating high intrasubject variability in distribution and clearance, AUC truncation should not be used.

2. Type of study: Fed
Design: Single-dose, two-way crossover in vivo
Strength: EQ1.5 mg Base
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comments: See comments above

Analyte to measure (in appropriate biological fluid): Cariprazine in plasma

Bioequivalence based on (90% CI): Cariprazine

Waiver request of in vivo testing: EQ 3 mg Base, EQ 4.5 mg Base, and EQ 6.0 mg Base strengths based on (i) acceptable bioequivalence studies on the EQ 1.5 mg Base strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

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.