

Draft Guidance on Pimavanserin Tartrate

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover in vivo
Strength: EQ 17 mg Base at a dose of 34 mg (2x EQ 17 mg Base)
Subjects: Healthy males, and non-pregnant and non-lactating females, general population.
Comments: 1) Pimavanserin prolongs the QT interval. Serial electrocardiogram (ECG) monitoring is recommended pre-dose and during the studies for all subjects, and avoid using drugs known to prolong QT interval; 2) Pimavanserin and its major active metabolite (N-desmethylated metabolite AC-279) have long terminal elimination half-lives (>24 hours). Per the FDA Guidance for Industry: Bioequivalence (BE) Studies with Pharmacokinetic Endpoints for Drugs Submitted Under an ANDA (posted in 2013), applicants should ensure adequate washout periods between treatments in the crossover studies to avoid the carry-over from the first period. Alternatively, the applicants may also consider using a parallel study design for the drug with a long half-life. For long half-life drug products with low intra-subject variability in distribution and clearance, an AUC truncated to 72 hours may be used in place of AUC_{0-t} or $AUC_{0-\infty}$. 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. The applicants should collect sufficient blood samples in the bioequivalence studies to adequately characterize the peak concentration (C_{max}) and time to reach peak concentration (t_{max}).
2. Type of study: Fed
Design: Single-dose, two-way crossover in vivo
Strength: EQ 17 mg Base at a dose of 34 mg (2x EQ 17 mg Base)
Subjects: Healthy males, and non-pregnant and non-lactating females, general population.
Comments: See comments above.

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

Bioequivalence based on (90% CI): Pimavanserin

Waiver request of in-vivo testing: Not applicable

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 (ANDA).