

Draft Guidance on Ivabradine Hydrochloride

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover in vivo
Strength: EQ 7.5 mg Base
Subjects: Healthy males and nonpregnant, non-lactating females, general population
Comments: Female subjects should not be pregnant, and should practice abstinence or contraception during the study, if applicable.
2. Type of study: Fed
Design: Single-dose, two-way crossover in vivo
Strength: EQ 7.5 mg Base
Subjects: Healthy males and nonpregnant females, general population.
Comments: See comments above

Analytes to measure (in appropriate biological fluid): Ivabradine and its active metabolite, N-desmethylated derivative (S18982), in plasma

Submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and C_{max} .

Bioequivalence based on (90% CI): Ivabradine

Waiver request of in-vivo testing: EQ 5 mg Base based on (i) acceptable bioequivalence studies on the 7.5 mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro disintegration 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 website 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.

The 5 mg Ivabradine Hydrochloride tablets are scored. For additional information on the evaluation of scored tablets, refer to the FDA Guidance on "Tablet Scoring: Nomenclature, Labeling, and Data for Evaluation" issued in March 2013 at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM269921.pdf>.