Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Infigratinib Phosphate

February 2023

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

Active Ingredient: Infigratinib phosphate

Dosage Form; Route: Capsule; oral

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 100 mg
   Subjects: Healthy males and females not of reproductive potential
   Additional comments: Perform a comprehensive ophthalmological examination prior to enrollment and exclude subjects with ophthalmological abnormalities. Male subjects with female partners of reproductive potential should use effective contraception during the study and for one month after the final dose. Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of infigratinib. Alternatively, a parallel study design may be considered.

Analytes to measure: Infigratinib and its active metabolite, BHS697, in plasma

Bioequivalence based on (90% CI): Infigratinib

Submit the metabolite data of BHS697 as supportive evidence of comparable therapeutic outcome. For 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 Cmax.

Waiver request of in vivo testing: 25 mg strength based on (i) acceptable bioequivalence study on the 100 mg strength, (ii) acceptable in vitro dissolution testing between two strengths, and (iii) proportional similarity of the formulations between two 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 applications.

Unique Agency Identifier: PSG_214622