Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Nilotinib Hydrochloride

February 2024

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form: Capsule

Route: Oral

Strengths: EQ 50 mg Base, EQ 150 mg Base, EQ 200 mg Base

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: EQ 200 mg Base
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: Exclude subjects with risk factors for prolonged QTc interval and Torsades de Pointes. Monitor electrocardiograms during the study. Exclude subjects with abnormal liver function tests or blood counts. Subjects should avoid consuming dietary supplements, fruits (e.g., grapefruit, Seville oranges), and products containing these fruits that may affect the exposure of nilotinib for a sufficient time prior to and during the study. Female subjects of reproductive potential should use effective contraception during the study and for 14 days after the final dose. Male subjects of reproductive potential and their female partners should use effective contraception during the study and for 14 days after the final dose.

Analyte to measure: Nilotinib in plasma

Bioequivalence based on (90% CI): Nilotinib

Waiver request of in vivo testing: EQ 50 mg Base and EQ 150 mg Base strengths based on (i) acceptable bioequivalence study on the EQ 200 mg Base 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 and reference products. Specifications will be determined upon review of the abbreviated new drug application.

Document History: Recommended April 2010; Revised July 2014, February 2024

Unique Agency Identifier: PSG_022068