Contains Nonbinding Recommendations

Draft Guidance on Dacomitinib

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 45 mg
   Subjects: Healthy adult males, and healthy adult non-pregnant, non-lactating females
   Additional comments: 1) Ensure adequate washout periods between treatments in the crossover studies due to dacomitinib's long terminal elimination half-life. A parallel study design may also be used due to the dacomitinib's long half-life. For either a crossover or a parallel study, sample collection time should be adequate to ensure completion of gastrointestinal transit of the drug product and absorption of the drug substance. Collect sufficient blood samples in the bioequivalence studies to adequately characterize the peak concentration and time to reach peak concentration. 2) Advise females of reproductive potential to use effective contraception during treatment with dacomitinib and for 17 days after the last dose of dacomitinib.

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2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 45 mg
   Subjects: Healthy adult males, and healthy adult non-pregnant, non-lactating females
   Additional comments: See comments above

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

Bioequivalence based on (90% CI): Dacomitinib

Waiver request of in vivo testing: 15 mg and 30 mg based on (i) acceptable bioequivalence studies on the 45 mg 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 for each strength of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.