Contains Nonbinding Recommendations

Draft Guidance on Ticagrelor

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

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: 90 mg
   Subjects: Males and females (non-pregnant), general population.
   Additional comments: None

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2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 90 mg
   Subjects: Males and females (non-pregnant), general population.
   Additional comments: None

Analytes to measure (in appropriate biological fluid): Ticagrelor and its active metabolite, AR-C124910XX in plasma

Applicants should submit data on ticagrelor's active metabolite (AR-C124910XX) 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 Cmax.

Bioequivalence based on (90% CI): Ticagrelor

Waiver request of in vivo testing: 60 mg strength based on (i) acceptable bioequivalence studies on the 90 mg strength, (ii) proportional similarity of the formulations between both strengths, and (iii) acceptable in vitro dissolution testing of both 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 each of both strengths of the test and

reference products. Specifications will be determined upon review of the abbreviated new drug application (ANDA).

Product-specific testing conditions for in vitro feeding tube studies:

The approved labeling for the reference product states that the product may be administered by a nasogastric (NG) tube (8 French or larger). Conduct the in vitro feeding tube studies including comparative recovery testing and sedimentation volume testing. In the preparation of feeding tube administration, crush the tablet for 60 seconds using a mortar and pestle and add the dispersion medium to the mortar and stir for 60 seconds using the pestle. Refer to the Lansoprazole Delayed-Release Orally Disintegrating Tablet Draft Guidance for additional information regarding procedures of in vitro feeding tube studies.

Testing tube: NG tube (8 French)

Testing strength: Two 90 mg tablets (180 mg dose)

Dispersion medium: 50 mL water

Incubation time: 0 and 120 minutes