Contains Nonbinding Recommendations

Draft Guidance on Aspirin; Omeprazole

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Delayed release tablet; oral

Recommended Studies: Two studies

1. Type of study**:** Fasting
   Design: Single-dose, two-way crossover *in vivo*
   Strength: 325 mg/ 40 mg
   Subjects: Males, non-pregnant females, general population
   Additional Comments: Applicants may consider using a reference-scaled average bioequivalence approach for the highly variable component of this drug product, aspirin. Provide evidence, from the studies, of high variability in the bioequivalence parameters, AUC and/or Cmax (i.e., within-subject variability > 30%) when using this approach. For general information on this approach, please refer to the Guidance on Progesterone Capsules.

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2. Type of study: Fed
   Design: Single-dose, two-way crossover *in vivo*
   Strength: 325 mg/ 40 mg
   Subjects: Healthy males, nonpregnant females, general population
   Additional Comments: Please see additional comment above.

Analytes to measure (in appropriate biological fluid): Acetylsalicylic acid, its active metabolite salicylic acid, and omeprazole in plasma
Please 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): Acetylsalicylic acid and omeprazole.
If there are not enough subjects having sufficient data to estimate the acetylsalicylic acid PK parameters under fed condition, bioequivalence evaluation may be based on the salicylic acid and omeprazole data.

Waiver request of *in-vivo* testing: 81 mg/40 mg strength, based on (i) acceptable bioequivalence studies on the 325 mg/ 40 mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. Please refer to the Mirtazapine Tablet Guidance for additional information regarding waivers of in-vivo testing.

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 (ANDA).