Contains Nonbinding Recommendations

Draft Guidance on Olsalazine Sodium

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Capsule; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in vivo
   Strength: 250 mg
   Subjects: Males and non-pregnant, non-lactating females, general population
   Additional comments: Use the lowest single dose possible to obtain accurate pharmacokinetic parameters for both olsalazine and mesalamine.

   Enroll enough subjects to achieve adequate statistical power to demonstrate bioequivalence to the reference listed drug. A pilot study may be necessary to assist in the determination of the appropriate number of subjects to enroll in the pivotal study. Refer to Appendix C of the Guidance for Industry, *Statistical Approaches to Establishing Bioequivalence*.

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2. Type of study: Fed
   Design: Single-dose, two-way crossover in vivo
   Strength: 250 mg
   Subjects: Males and non-pregnant, non-lactating females, general population
   Additional comments: See comments above

Analytes to measure (in appropriate biological fluid): Olsalazine and mesalamine in plasma

Bioequivalence based on (90% CI): Olsalazine and mesalamine

Waiver request of in-vivo testing: Not applicable

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 the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.

In addition, perform dissolution testing over a range of pH values comparing the test and reference products. Various pH conditions should be studied to approximate the pH conditions that olsalazine sodium capsules will be subjected to in the gastrointestinal tract. Therefore, the following pH conditions should be used on 12 dosage units of the test and reference products. The f2 metric should be used for dissolution profile comparisons:

Apparatus: USP Apparatus I (basket)
Speed: 100 rpm
Medium: 0.1N HCl; pH 4.5 phosphate buffer; pH 6.8 phosphate buffer,
Volume: 900 mL
Sampling Times: 10, 20, 30, 45, and 60 minutes and until at least 80% of the labeled content is dissolved.