Contains Nonbinding Recommendations

Draft Guidance on Sulfasalazine

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

Active ingredient: Sulfasalazine

Form/Route: Tablet, Delayed Release/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 500 mg
   Subjects: Healthy males and nonpregnant females, general population.
   Additional Comments:

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2. Type of study: Fed
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 500 mg
   Subjects: Healthy males and nonpregnant females, general population.
   Additional Comments:

Analytes to measure (in appropriate biological fluid): Sulfasalazine, and the metabolites sulfapyridine and 5-aminosalicylic (5-ASA) acid (mesalamine) in plasma

Bioequivalence based on (90% CI): Sulfasalazine and 5-Aminosalicylic Acid

Please submit the metabolite sulfapyridine 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 Cmax.

Waiver request of in-vivo testing: Not applicable

Dissolution test method and sampling times:

Please note that a **Dissolution Methods Database** is available to the public at the OGD website at http://www.accessdata.fda.gov/scripts/cder/dissolution/. Please find the dissolution information for this product at this website. Please 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 application.

Because sulfasalazine acts locally in the gastro-intestinal (GI) tract (rather than systemically), evaluation of dissolution is important in determining whether an equivalent amount of drug from each formulation, test and reference, is delivered to the sites of activity in the GI tract. Therefore, in addition to the method above, dissolution profiles on 12 dosage units each of test and reference product generated using USP Apparatus I at 100 rpm in four dissolution media (pH 1.2, and pH 4.5, 6.8, and 7.4 buffer) should be submitted in the application. Agitation speeds may be increased if appropriate.