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Draft Guidance on Mesalamine

December 2025

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

Active Ingredient:	Mesalamine
Dosage Form:	Tablet, delayed release
Route:	Oral
Strength:	1.2 gm
Recommended Studies:	Two in vivo bioequivalence studies with pharmacokinetic endpoints and one in vitro comparative dissolution study

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 1.2 gm
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comment:
   - A replicate crossover study design (partial or fully replicate) is acceptable whether the reference listed drug (RLD) is a highly variable drug or not. Applicants may consider using a reference-scaled average bioequivalence approach for mesalamine. If using this approach, provide evidence of high variability in the pharmacokinetic parameters (i.e., within-subject variability ≥30%) for the RLD. For detailed information on this approach, refer to the most recent version of the guidance for industry *Bioequivalence Studies with Pharmacokinetic Endpoints for Drugs Submitted Under an Abbreviated New Drug Application*.[a]

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 1.2 gm
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comment: See comment above.

Analyte to measure: Mesalamine in plasma

Bioequivalence based on (90% CI): Mesalamine

Extensive blood samples should be collected around time to maximum concentration to accurately estimate the maximum plasma concentration (C_{max}). At least four consecutive non-zero measurements of concentrations are recommended for area under the concentration (AUC) time curve from 8 to 48 hours (AUC_{8-48}).

For both fasting and fed studies, the following pharmacokinetic parameters are recommended: Log-transformed AUC_{8-48}, AUC from hour 0 to the last measurable time point (AUC_{0-t}), and C_{max}.

Because AUC_{0-t} is recommended in place of AUC from hour 0 extrapolated to infinite time, the last sampling time point should be at least 72 hours.

3. Type of study: In vitro comparative dissolution study

Strength:	1.2 gm
Apparatus:	United States Pharmacopoeia (USP) Apparatus 2 (paddle)
Pretreatment Stage 1:	2 hours in 0.1 N HCl at 100 rpm (750 mL)
Pretreatment Stage 2:	1 hour in pH 6.4 phosphate buffer at 100 rpm (950 mL)
Evaluation Stage:	Each of (1) pH 6.5 phosphate buffer at 100 rpm (2) pH 6.8 phosphate buffer at 100 rpm (3) pH 7.2 phosphate buffer at 100 rpm (4) pH 7.5 phosphate buffer at 100 rpm
Volume:	960 mL
Temperature:	37°C
Sampling times:	1, 2, 3, 4, 5, 6, and 8 hours or as needed for profile comparison
Additional comments:	The applicant should use at least 24 dosage units of the test product and at least 2 lots of the RLD (12 dosage units per lot) per test. The f2 metric should be used to compare dissolution profiles. The results from comparative dissolution studies at pH 6.5 and pH 6.8 are used as supportive evidence for bioequivalence assessment to confirm that there is no early release for the test product.

Additional Strengths: Not applicable

Dissolution test method and sampling times: For modified release drug products, applicants should develop specific discriminating dissolution methods. Alternatively, applicants may use the dissolution method set forth in any related official USP drug product monograph, or in the FDA's database, http://www.accessdata.fda.gov/scripts/cder/dissolution/, provided that applicants submit adequate dissolution data supporting the discriminating ability of such a method. If a new dissolution method is developed, submit the dissolution method development and validation report with the complete information/data supporting the proposed method. Conduct comparative dissolution testing on 24 dosage units for the test product and at least 2 lots of RLD (12 dosage units from each lot). Specifications will be determined upon review of the abbreviated new drug application.

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[a] For the most recent version of a guidance, check the FDA guidance website at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.