

Contains Nonbinding Recommendations

Draft – Not for Implementation

## Draft Guidance on Apremilast

May 2026

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

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<b>Active Ingredient:</b>	Apremilast
<b>Dosage Form:</b>	Tablet, extended release
<b>Route:</b>	Oral
<b>Strength:</b>	75 mg
<b>Reference Listed Drug:</b>	NDA 210745
<b>Recommended Studies:</b>	Two in vivo bioequivalence studies with pharmacokinetic endpoints
1.	Class of study: Bioequivalence Type of study: Fasting Design: Single-dose, two-treatment, two-period crossover in vivo Strength: 75 mg Subjects: Healthy males and non-pregnant, non-lactating females
2.	Class of study: Bioequivalence Type of study: Fed Design: Single-dose, two-treatment, two-period crossover in vivo Strength: 75 mg Subjects: Healthy males and non-pregnant, non-lactating females
<b>Analyte to measure:</b>	Apremilast in plasma
<b>Bioequivalence based on (90% CI):</b>	Apremilast
<b>Additional strengths:</b>	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 United States Pharmacopeia (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 12 dosage units for each of the test product and reference listed drug (RLD).<sup>1</sup> Specifications will be determined upon review of the abbreviated new drug application.

In addition to the method above, submit dissolution profiles on 12 dosage units for each of the test product and RLD generated using USP Apparatus 1 at 100 rpm and/or Apparatus 2 at 50 rpm in at least three dissolution media (e.g., pH 1.2, 4.5 and 6.8 buffer). Agitation speeds may be increased if appropriate. It is acceptable to add a small amount of surfactant if necessary. Include early sampling times of 1, 2, and 4 hours and continue every 2 hours until at least 80% of the drug is released to provide assurance against premature release of drug (dose dumping) from the formulation.

**Alcohol dose dumping studies:** Due to concerns of dose dumping of drug from this product when taken with alcohol, conduct additional dissolution testing using various concentrations of ethanol in the dissolution medium as follows:

Testing conditions: 900 mL, 0.1N HCl, USP Apparatus 2 (paddle) at 75 rpm, with or without alcohol

Test 1: 12 units tested according to the proposed method (with 0.1 N HCl) with data collected every 15 minutes for a total of 2 hours

Test 2: 12 units analyzed by substituting 5% (v/v) of test medium with Alcohol USP and data collection every 15 minutes for a total of 2 hours

Test 3: 12 units analyzed by substituting 20% (v/v) of test medium with Alcohol USP and data collection every 15 minutes for a total of 2 hours

Test 4: 12 units analyzed by substituting 40% (v/v) of test medium with Alcohol USP and data collection every 15 minutes for a total of 2 hours

Conduct testing on both test product and RLD accordingly, and provide data on individual unit, means, range and %CV.

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**Document History:** Recommended May 2026

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<sup>1</sup> If the RLD is not available, refer to the most recent version of the guidance for industry *Referencing Approved Drug Products in ANDA Submissions*.