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Draft Guidance on Tofacitinib Citrate

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Active Ingredient:	Tofacitinib citrate
Dosage Form:	Tablet
Route:	Oral
Strengths:	EQ 5 mg Base | EQ 10 mg Base
Reference Listed Drug:	NDA 203214
Recommended Studies:	Two options: (I) Biopharmaceutics Classification System (BCS)-based biowaiver, or (II) one in vivo bioequivalence study with pharmacokinetic endpoints

Option I: BCS Class III-based biowaiver

BCS-III waiver: A waiver request of in vivo testing for both strengths of this product may be considered provided that the appropriate documentation regarding high solubility, very rapid dissolution of the test product and reference listed drug (RLD), and the test product formulation is qualitatively the same and quantitatively very similar as detailed in the guidance for industry *M9 Biopharmaceutics Classification System-Based Biowaivers*[a] is submitted in the application. Applicants may use the information contained in the approved labeling of the RLD. Peer-reviewed articles may not contain the necessary details of the testing for the Agency to make a judgement regarding the quality of the studies. A decision regarding the acceptability of the waiver request can only be made upon assessment of the data submitted in the application.

Option II: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Class of study: Bioequivalence
   Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: EQ 10 mg Base
   Subjects: Healthy males and non-pregnant, non-lactating females
   Safety recommendations:
   - Exclude subjects with latent tuberculosis, abnormal liver function tests or complete blood counts.
   - Subjects should be informed not to use live vaccines immediately prior to or during the study.
   - Monitor for signs and symptoms of infection during the study.

Analyte to measure: Tofacitinib in plasma

Bioequivalence based on (90% CI): Tofacitinib

Waiver request of in vivo testing of additional strength: Justification based on (i) an acceptable bioequivalence study on the EQ 10 mg Base strength, (ii) acceptable comparative in vitro dissolution studies between the additional strength and the EQ 10 mg Base strength using 12 units per strength, and (iii) proportional similarity of the formulations between both strengths

Dissolution: Dissolution tests should be included for quality control and to support a waiver request of in vivo testing of the additional strength. For the quality control dissolution method, provide a dissolution method development report for the test product containing information and data that demonstrate appropriateness of the selected dissolution method[1] and sampling times, such as the discriminating ability to detect changes in critical quality attributes that could potentially impact drug product performance.

For drug products containing high solubility drug substances that meet the rapidly dissolving criteria, demonstration of discriminating ability may not be needed. For additional information, refer to the guidance for industry *Dissolution Testing and Acceptance Criteria for Immediate-Release Solid Oral Dosage Form Drug Products Containing High Solubility Drug Substances*.[a]

Document History: Recommended December 2014; Revised May 2019, October 2024, May 2026

[a] We update guidanes periodically. For the most recent version of a guidance, refer to the FDA guidance webpage at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[1] Applicant-developed, United States Pharmacopeia (USP) drug product monograph or Dissolution Methods database, https://www.accessdata.fda.gov/scripts/cder/dissolution/index.cfm