Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Rilzabrutinib

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form: Tablet

Route: Oral

Strength: 400 mg

Reference Listed Drug: NDA 219685

Recommended Study: 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: 400 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Safety recommendations:
   - Exclude subjects with abnormal liver function tests.
   - Females of reproductive potential should use non-hormonal contraception during the study and continue to use effective contraception for 1 week after the last dose.

   Study design recommendation:
   - Subjects should avoid consuming dietary supplements, fruits (e.g., grapefruit, starfruit, Seville oranges) and products containing these fruits that may affect the exposure of rilzabrutinib for a sufficient time prior to and during the study.

Analyte to measure: Rilzabrutinib in plasma

Bioequivalence based on (90% CI): Rilzabrutinib

Dissolution: Dissolution test(s) should be included for quality control. 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.

Document History: Recommended August 2026

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