Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Amlodipine Besylate; Indapamide; Telmisartan

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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 Ingredients:	Amlodipine besylate; Indapamide; Telmisartan
Dosage Form:	Tablet
Route:	Oral
Strengths:	EQ 1.25 mg Base; 0.625 mg; 10 mg | EQ 2.5 mg Base; 1.25 mg; 20 mg | EQ 5 mg Base; 2.5 mg; 40 mg
Reference Listed Drug:	NDA 219423
Recommended Studies:	Three 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: EQ 5 mg Base; 2.5 mg; 40 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Safety recommendations:
   - Subjects should remain in a semi-recumbent or supine position for up to eight hours after dosing to prevent symptomatic hypotension. Monitor vital signs and adverse events associated with hypotension.
   - When transitioning to standing position, subjects should be closely observed for blood pressure changes and/or symptoms of hypotension (e.g., lightheadedness, dizziness, and/or faintness).

Study design recommendations:

- $AUC_{(0\text{-}72h)}$ may be used in place of $AUC_{(0\text{-}t)}$ for comparing the extent of absorption due to amlodipine's long half-life. Ensure adequate washout periods between treatments in the crossover study.
- Alternatively, a parallel study design may be considered.
- Applicants may consider using a reference-scaled average bioequivalence approach for telmisartan. If using this approach, provide evidence of high variability in the pharmacokinetic parameters (i.e., within-subject variability ≥30%) for the reference listed drug (RLD). For detailed information on this approach, refer to the guidance for industry *Bioequivalence Studies With Pharmacokinetic Endpoints for Drugs Submitted Under an ANDA*.[a]

2. Class of study: Bioequivalence
Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: EQ 5 mg Base; 2.5 mg; 40 mg
Subjects: Healthy males and non-pregnant, non-lactating females
Study design recommendations:
    - See recommendations under Study #1.
    - In vivo testing of the EQ 5 mg Base; 2.5 mg; 40 mg strength under the fed conditions may be waived when the test product has the same product design as the RLD including manufacturing techniques for the telmisartan component. The critical excipient should be qualitatively the same and quantitatively similar, e.g., within ±10% of the amount of polyvinyl pyrrolidone for the telmisartan component in the RLD.

3. Class of study: Bioequivalence
Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: EQ 1.25 mg Base; 0.625 mg; 10 mg
Subjects: Healthy males and non-pregnant, non-lactating females
Study design recommendations:
    - See recommendations under Study #1.
    - In vivo testing of the EQ 1.25 mg Base; 0.625 mg; 10 mg strength under the fasting condition may be waived when the test product has the same product design as the RLD including manufacturing techniques for the telmisartan component. The critical excipient should be qualitatively the same and quantitatively similar, e.g., within ±10% of the amount of polyvinyl pyrrolidone for the telmisartan component in the RLD.

Analytes to measure: Amlodipine and telmisartan in plasma, and indapamide in whole blood

Bioequivalence based on (90% CI): Amlodipine, indapamide, and telmisartan

Waiver request of in vivo testing of additional strength: Justification for EQ 2.5 mg Base; 1.25 mg; 20 mg strength based on (i) acceptable bioequivalence studies on the EQ 1.25 mg Base; 0.625 mg; 10 mg strength and EQ 5 mg Base; 2.5 mg; 40 mg strength, (ii) acceptable comparative in vitro dissolution studies using 12 units per strength, and (iii) acceptable proportional similarity of the formulations between additional strength and the bio-strengths

Dissolution: Dissolution test(s) should be included for quality control and to support a waiver request of in vivo testing of additional strengths. 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.

Document History: Recommended May 2026

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

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