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Draft – Not for Implementation

Draft Guidance on Tizanidine Hydrochloride

February 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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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:	Tizanidine hydrochloride
Dosage Form:	Capsule
Route:	Oral
Strengths:	EQ 2 mg Base, EQ 3 mg Base,[1] EQ 4 mg Base, EQ 6 mg Base, EQ 8 mg Base[2]
Recommended Studies:	Two in vivo bioequivalence studies with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: EQ 8 mg Base
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments:
   - Subjects should be kept in a sitting position for at least six hours after dosing. Vital signs and alertness should be monitored before allowing subjects to resume ambulation. Exclude subjects with a history of hypotension or with abnormal liver function tests. Exclude geriatric subjects due to increased risk of hypotension and central nervous system adverse events. Exclude current or recent smokers (i.e., user of nicotine containing products within three months prior to dosing) due to potential impact of smoking on pharmacokinetics of tizanidine.

[1] Strength identified is the subject of an approved suitability petition (FDA-2025-P-0268).
[2] Strength identified is the subject of an approved suitability petition (FDA-2021-P-0495).

- Applicants may consider one of the following approaches which is appropriate at time of the study:
    - Conduct the study by testing one tizanidine hydrochloride capsule (1 × EQ 8 mg Base) of the test product compared to two tizanidine hydrochloride capsules (2 × EQ 4 mg Base) of the reference listed drug (RLD).[3]
    - Conduct the study by testing one tizanidine hydrochloride capsule (1 × EQ 8 mg Base) of the test product compared to one tizanidine hydrochloride capsule (1 × EQ 8 mg Base) of the reference standard (RS), provided there is an approved petitioned abbreviated new drug application for tizanidine hydrochloride capsules, EQ 8 mg Base, designated as the RS.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: EQ 8 mg Base
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments: See comments above.

Analyte to measure: Tizanidine in plasma

Bioequivalence based on (90% CI): Tizanidine

Waiver request of in vivo testing additional strengths: Justification based on (i) acceptable bioequivalence studies on the EQ 8 mg Base strength, (ii) acceptable comparative in vitro dissolution studies between additional strength**s** and the EQ 8 mg Base strength using 12 units per strength, and (iii) proportional similarity of the formulations across all strengths

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

Dissolution test method and sampling times: Provide a dissolution method development report for the test product containing information and data that demonstrate appropriateness of the selected dissolution method[4] 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 most recent version of the guidance for industry *Dissolution Testing and Acceptance Criteria for Immediate-Release Solid Oral Dosage Form Drug Products Containing High Solubility Drug Substances.*[a]

[3] If the RLD is not available, refer to the most recent version of the guidance for industry *Referencing Approved Drug Products in ANDA Submissions.*
[4] Applicant-developed, United States Pharmacopeia drug product monograph or Dissolution Methods database, https://www.accessdata.fda.gov/scripts/cder/dissolution/index.cfm

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