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Tizanidine Tablets

DEFINITION
Tizanidine Tablets contain Tizanidine Hydrochloride equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of tizanidine ($C_9H_8ClN_5S$).

IDENTIFICATION
- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY
- **Procedure**

Solution A: Water and phosphoric acid (44:6)

Buffer: 3.5 g/L of sodium 1-pentanesulfonate. Adjust with *Solution A* or 1 N sodium hydroxide to a pH of 3.0.

Mobile phase: Acetonitrile and *Buffer* (20:80)

Tizanidine related compound A solution: 0.1 mg/mL of USP Tizanidine Related Compound A RS in methanol

Tizanidine related compound B solution: 0.1 mg/mL of USP Tizanidine Related Compound B RS in methanol

Tizanidine related compound C solution: 0.1 mg/mL of USP Tizanidine Related Compound C RS in methanol

System suitability solution: Transfer 23 mg of USP Tizanidine Hydrochloride RS to a 100-mL volumetric flask, and add 20 mL of *Mobile phase* and 10 mL each of *Tizanidine related compound A solution*, *Tizanidine related compound B solution*, and *Tizanidine related compound C solution*. Sonicate to dissolve the USP Tizanidine Hydrochloride RS, and dilute with *Mobile phase* to volume.

Standard solution: 0.046 mg/mL of USP Tizanidine Hydrochloride RS in *Mobile phase*

Sample solution: Transfer a weighed portion of finely powdered Tablets (NLT 20), equivalent to 20 mg of tizanidine, to a 500-mL volumetric flask. Add 250 mL of *Buffer* solution, sonicate for 15 min with occasional shaking, and shake by mechanical means for 15 min. Add 100 mL of acetonitrile, and mix. Allow to cool, and dilute with *Buffer* solution to volume. Centrifuge a portion of this solution at 2000 rpm or higher for 10 min. Pass a portion of this solution through a filter with a 0.45-µm or finer pore size, and use the filtrate.

Chromatographic system
(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 230 nm. For *Identification B*, use a diode array detector in the range of 210–400 nm.

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 50°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[Note—The relative retention times are listed in *Table 1*.]

Suitability requirements

Resolution: NLT 4.0 between tizanidine and tizanidine related compound C; NLT 4.0 between tizanidine and tizanidine related compound B, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of tizanidine ($C_9H_8ClN_5S$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Tizanidine Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of tizanidine in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of tizanidine, 253.71

M_{r2} = molecular weight of tizanidine hydrochloride, 290.17

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Test 1

Medium: 0.1 N hydrochloric acid; 500 mL

Apparatus 1: 100 rpm

Time: 15 min

Solution A, Buffer, and **Mobile phase:** Prepare as directed in the *Assay*.

Standard solution: (*L*/500) mg/mL of USP Tizanidine Hydrochloride RS in *Medium*, where *L* is the label claim, in mg

Sample solution: Sample per *Dissolution ⟨711⟩*. Dilute with *Medium* to a concentration that is similar to the *Standard solution*.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 230 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 50°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of tizanidine ($C_9H_8ClN_5S$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (1/L) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of tizanidine from the *Sample solution*

r_S = peak response of tizanidine from the *Standard solution*

C_S = concentration of USP Tizanidine Hydrochloride RS in the *Standard solution* (mg/mL)

V = volume of dissolution *Medium*, 500 mL

L = label claim, in mg

M_{r1} = molecular weight of tizanidine, 253.71

M_{r2} = molecular weight of tizanidine hydrochloride, 290.17

Tolerances: NLT 80% (*Q*) of the labeled amount of tizanidine ($C_9H_8ClN_5S$) is dissolved.

Test 2

[NOTE—If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 2*.]

Medium: 0.1 N hydrochloric acid; 500 mL, deaerated

Apparatus 1: 100 rpm

Time: 30 min

Standard solution: (*L*/500) mg/mL of USP Tizanidine Hydrochloride RS in *Medium*, where *L* is the label claim, in mg

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV

Analytical wavelength: 228 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of tizanidine ($C_9H_8ClN_5S$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times (1/L) \times (M_{r1}/M_{r2}) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of USP Tizanidine Hydrochloride RS in the *Standard solution* (mg/mL)

V = volume of dissolution *Medium*, 500 mL

L = label claim, in mg

M_{r1} = molecular weight of tizanidine, 253.71

M_{r2} = molecular weight of tizanidine hydrochloride, 290.17

Tolerances: NLT 80% (*Q*) of the labeled amount of tizanidine ($C_9H_8ClN_5S$) is dissolved.

IMPURITIES

• **Organic Impurities**

Solution A, Buffer, Mobile phase, System suitability solution, Standard solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Sample solution: Transfer a weighed portion of finely powdered Tablets (NLT 20), equivalent to 20 mg of tizanidine, to a 100-mL volumetric flask. Add about 50 mL of *Buffer* solution, sonicate for about 15 min with occasional shaking, and shake by mechanical means for 15 min. Add 20 mL of acetonitrile, and mix. Allow to cool, dilute with *Buffer* solution to volume, and mix. Centrifuge a portion of this solution at 2000 rpm or higher for 10 min. Pass a portion of this solution through a filter with a 0.45-µm or finer pore size, and use the filtrate.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times (1/F) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response of tizanidine from the *Standard solution*

C_S = concentration of USP Tizanidine Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of tizanidine in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of tizanidine, 253.71

M_{r2} = molecular weight of tizanidine hydrochloride, 290.17

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Tizanidine related compound C[a]	0.8	—	—
Tizanidine	1.0	—	—
Tizanidine related compound B[a]	1.4	—	—
Tizanidine related compound A	10.2	1.1	0.2
Any unspecified degradation product	—	1.0	0.2
Total impurities	—	—	0.5

[a] Process impurity included for peak identification purposes only. Controlled in the drug substance.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers, and store at controlled room temperature.
- **Labeling:** When more than one *Dissolution* test is given, the labeling states the test used only if *Test 1* is not used.
- **USP Reference Standards** ⟨11⟩

USP Tizanidine Hydrochloride RS

USP Tizanidine Related Compound A RS

4-Amino-5-chloro-2,1,3-benzothiadiazole.

$C_6H_4ClN_3S$ 185.63

USP Tizanidine Related Compound B RS

N-Acetyltizanidine.

$C_{11}H_{10}ClN_5OS$ 295.75

USP Tizanidine Related Compound C RS

1-Acetylimidazolidine-2-thione.

$C_5H_8N_2OS$ 144.19

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
TIZANIDINE TABLETS	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

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