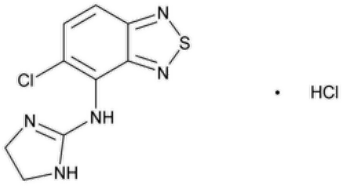
Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-May-2021
Document Type: USP Monographs
DocId: GUID-85484A93-7C4F-4A60-96FE-0FEE3557CA1D_5_en-US
DOI: https://doi.org/10.31003/USPNF_M83740_05_01
DOI Ref: ue5dt

Tizanidine Hydrochloride



• HCl

$C_9H_8ClN_5S \cdot HCl$ 290.17

2,1,3-Benzothiadiazol-4-amine, 5-chloro-*N*-(4,5-dihydro-1*H*-imidazol-2-yl)-, monohydrochloride;

5-Chloro-4-(2-imidazolin-2-ylamino)-2,1,3-benzothiadiazole monohydrochloride CAS RN®: 64461-82-1; UNII: B53E3NMY5C.

DEFINITION

Tizanidine Hydrochloride contains NLT 98.0% and NMT 102.0% of tizanidine hydrochloride ($C_9H_8ClN_5S \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

• **A.** **Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution,* as obtained in the *Assay*.

Change to read:

• **C.** **Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Chloride***

Sample solution: 10 mg/mL

Acceptance criteria: Meets the requirements ▲▲ (USP 1-May-2021)

ASSAY

Change to read:

• **Procedure**

Buffer: 6.8 g/L of monobasic potassium phosphate. Adjust with 5.3 N potassium hydroxide to a pH of 7.5 ± 0.05.

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

System suitability solution: 46 µg/mL of USP Tizanidine Hydrochloride RS and 0.12 µg/mL of USP Tizanidine Related Compound C RS in *Mobile phase*

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

Sample solution: 0.046 mg/mL of Tizanidine Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 4.6-mm × 15-cm; packing L7

Column temperature: 35°

Flow rate: 1 mL/min

Injection volume: 20 µL

▲**Run time:** NLT 2.3 times the retention time of tizanidine▲ (USP 1-May-2021)

System suitability

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

[Note—The relative retention times for tizanidine related compound C and tizanidine are 0.5 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 6 between tizanidine and tizanidine related compound C, *System suitability solution*

Tailing factor: NMT 2.0 for tizanidine, *Standard solution*

Relative standard deviation: NMT ▲0.73%▲ (USP 1-May-2021) *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of tizanidine hydrochloride ($C_9H_8ClN_5S \cdot HCl$) in the portion of Tizanidine Hydrochloride taken:

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

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

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

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

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

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

Change to read:

• **Organic Impurities**

Solution A: Water and phosphoric acid (88:12)

Buffer: 3.5 g/L of sodium 1-pentanesulfonate. Adjust with *Solution A* or 1 N sodium hydroxide to a pH of 3.0 ± 0.05.

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

System suitability stock solution: 0.1 mg/mL each of USP Tizanidine Related Compound A RS, USP Tizanidine Related Compound B RS, and USP Tizanidine Related Compound C RS in methanol

System suitability solution: 0.23 mg/mL of USP Tizanidine Hydrochloride RS, and 0.01 mg/mL each of USP Tizanidine Related Compound A RS, USP Tizanidine Related Compound B RS, and USP Tizanidine Related Compound C RS from *System suitability stock solution* in *Mobile phase*

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

Sample solution: 1.14 mg/mL of Tizanidine Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 4.6-mm × 25-cm; packing L1

Column temperature: 50°

Flow rate: 1 mL/min

Injection volume: 10 µL

▲**Run time:** NLT 11 times the retention time of tizanidine▲ (USP 1-May-2021)

System suitability

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

[Note—See *Table 1* for the relative retention times.]

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*

Column efficiency: NLT 5000 theoretical plates, *Standard 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 each impurity in the portion of Tizanidine Hydrochloride 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 area of each impurity from the *Sample solution*

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

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

C_U = concentration of Tizanidine Hydrochloride 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*. ▲Reporting threshold is 0.05%.▲ (USP 1-May-2021)

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Tizanidine related compound C	0.8	1.0	0.1
Tizanidine	1.0	—	—
Tizanidine related compound B	1.4	1.1	0.1
Tizanidine related compound A	10.2	1.1	0.1
▲Any▲ (USP 1-May-2021) individual unspecified impurity	—	1.0	0.1
Total impurities	—	—	0.3

SPECIFIC TESTS

• **pH** ⟨791⟩

Sample solution: 10 mg/mL

Acceptance criteria: 4.3–5.3

• **Loss on Drying** ⟨731⟩

Sample: 0.5 g

Analysis: Dry the *Sample* at 105° for 3 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store at room temperature.

Change to read:

• **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

▲5-Chloro-4-(1-acetyl-2-imidazolin-2-ylamino)-2,1,3-benzothiadiazole.▲ (USP 1-May-2021)

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

USP Tizanidine Related Compound C RS

1-Acetylimidazolidine-2-thione.

$C_5H_8N_2OS$ ▲144.19▲ (USP 1-May-2021)

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 45(2)

Current DocID: GUID-85484A93-7C4F-4A60-96FE-0FEE3557CA1D_5_en-US
DOI: https://doi.org/10.31003/USPNF_M83740_05_01
DOI ref: ue5dt