Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-May-2023
Document Type: USP Monographs
DocId: GUID-5BD7EA82-C83E-4EF2-AFEB-B31384EE744C_7_en-US
DOI: https://doi.org/10.31003/USPNF_M84492_07_01
DOI Ref: wos5l

Trazodone Hydrochloride Tablets

DEFINITION
Trazodone Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of trazodone hydrochloride ($C_{19}H_{22}ClN_5O \cdot HCl$).

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

ASSAY
Change to read:
- **Procedure**

Buffer: 1.15 g/L of monobasic ammonium phosphate, adjusted with sodium hydroxide to a pH of 6.0

Mobile phase: Methanol and *Buffer* (75:25)

Standard solution: 0.1 mg/mL of USP Trazodone Hydrochloride RS in 0.01 N hydrochloric acid TS

Sample solution: Nominally 0.1 mg/mL of trazodone hydrochloride from finely powdered Tablets (NLT 20). Transfer a suitable quantity of the powder to a suitable volumetric flask. Dissolve in 0.01 N hydrochloric acid TS and dilute with 0.01 N hydrochloric acid TS to volume. Sonicate for about 30 min, and pass through a suitable filter of 0.45-µm pore size.

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

Mode: LC

Detector: UV 246 nm. For *Identification A*, use a diode array detector in the range of 200–400 nm.

Column: 5-mm × 10-cm; 4-µm packing L1

Flow rate: 1.5 mL/min

Injection volume: 20 µL

Run time: NLT 4.5 times the retention time of trazodone

System suitability

Sample: *Standard solution*

Suitability requirements

▲Tailing factor: NMT 2.5▲ (USP 1-May-2023)

Relative standard deviation: NMT ▲1.0%▲ (USP 1-May-2023)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of trazodone hydrochloride ($C_{19}H_{22}ClN_5O \cdot HCl$) in the portion of Tablets taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Test 1

Medium: 0.01 N hydrochloric acid TS; 900 mL

Apparatus 2: 50 rpm

Time: 60 min

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

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of trazodone hydrochloride ($C_{19}H_{22}ClN_5O \cdot HCl$) dissolved:

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

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

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

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of trazodone hydrochloride ($C_{19}H_{22}ClN_5O \cdot HCl$) is dissolved.

Test 2: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 2*.

Medium: 0.01 N hydrochloric acid TS; ▲500▲ (USP 1-May-2023) mL

Apparatus 2: ▲75▲ (USP 1-May-2023) rpm

Time: ▲15▲ (USP 1-May-2023) min

Buffer: To each liter of water add 5 mL of triethylamine, and adjust with phosphoric acid to a pH of 3.0.

Mobile phase: Acetonitrile and *Buffer* (25:75)

Standard solution: ▲(L/500)▲ (USP 1-May-2023) mg/mL of USP Trazodone Hydrochloride RS in *Medium*, ▲where L is the label claim, in mg/Tablet.▲ (USP 1-May-2023) Sonicate if necessary.

Sample solution: Pass the solution through a suitable filter of 0.45-µm pore size. Discard the first 5 mL of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 246 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 45°

Flow rate: 1.5 mL/min

Injection volume: ▲5▲ (USP 1-May-2023) µL

Run time: NLT 1.6 times the retention time of trazodone

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 trazodone hydrochloride ($C_{19}H_{22}ClN_5O \cdot HCl$) dissolved:

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

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

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

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

V = volume of *Medium*, ▲500▲ (USP 1-May-2023) mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of trazodone hydrochloride ($C_{19}H_{22}ClN_5O \cdot HCl$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

Change to read:

• **Organic Impurities**

Solution A: 6.75 g/L of monobasic potassium phosphate. Add 1.0 mL of triethylamine for each liter of the solution, and mix.

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
5	90	10
30	60	40
35	60	40
60	42	58
63	30	70
78	30	70
78.1	90	10
90	90	10

Diluent: Methanol, water, and hydrochloric acid (650:350:3)

System suitability solution: 0.7 µg/mL of USP Trazodone Hydrochloride RS and 1.5 µg/mL of USP Trazodone Related Compound C RS in *Diluent*

Standard solution: 0.7 µg/mL of USP Trazodone Hydrochloride RS in *Diluent*

Sample solution: Nominally 500 µg/mL of trazodone ▲hydrochloride▲ (USP 1-May-2023) from finely powdered Tablets (NLT 20) prepared as follows. Transfer a portion of powdered Tablets (▲equivalent to▲ (USP 1-May-2023) NLT 50 mg ▲of trazodone hydrochloride▲ (USP 1-May-2023)) to a suitable volumetric flask. Add about 80% of the flask volume of *Diluent*, and sonicate for 10 min. Dilute with *Diluent* to volume. Pass a portion of the solution through a suitable membrane filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.0-mm × 15-cm; 3-µm packing L1

Flow rate: 0.7 mL/min

Injection volume: 10 µL

System suitability

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

[NOTE—See *Table 2* for the relative retention times.]

Suitability requirements

Resolution: NLT 2.5 between trazodone related compound C and trazodone, ▲▲ (USP 1-May-2023) *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

▲**Signal-to-noise ratio:** NLT 10, *Standard solution*▲ (USP 1-May-2023)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ▲any▲ (USP 1-May-2023) degradation product in the portion of Tablets taken:

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

r_U = peak response of ▲any▲ (USP 1-May-2023) degradation product from the *Sample solution*

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

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

C_U = nominal concentration of trazodone ▲hydrochloride▲ (USP 1-May-2023) in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 2*. ▲The reporting threshold is 0.1%.▲ (USP 1-May-2023)

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Triazolopyridinone[a,b]	0.1	—
Chlorophenylpiperazine[a,c]	0.6	—
Hydroxypropyl chlorophenylpiperazine[a,d]	0.7	—
Isotrazodone[a,e]	0.8	—
Trazodone related compound C[a]	0.97	—
Trazodone ▲▲ (USP 1-May-2023)	1.0	—
Trazodone dimer[a,f]	1.5	—
Trazodone related compound F[a,g]	1.6	—
Bispiperazine analog[a,h]	1.8	—
Bis(3-chlorophenyl)piperazine[a,i]	2.2	—
Any ▲▲ (USP 1-May-2023) unspecified degradation product	—	1.0
Total degradation products	—	2.0

[a] Process impurity included for identification only. Process impurities are controlled in the drug substance, and are not to be reported or included in the ▲total degradation products▲ (USP 1-May-2023) for the drug product.

[b] [1,2,4]Triazolo[4,3-*a*]pyridin-3(2*H*)-one.

[c] 1-(3-Chlorophenyl)piperazine.

[d] 3-[4-(3-Chlorophenyl)piperazin-1-yl]propan-1-ol.

[e] 1-{3-[4-(3-Chlorophenyl)piperazin-1-yl]propyl}-[1,2,4]triazolo[4,3-*a*]pyridin-1-ium-3-olate.

[f] 2,2'-{[Ethane-1,1-diylbis(3-chloro-4,1-phenylene)bis(piperazine-4,1-diyl)]bis(propane-3,1-diyl)}bis([1,2,4]triazolo[4,3-α]pyridin-3(2*H*)-one).

[g] 1-(3-Chlorophenyl)-4-(3-chloropropyl)piperazine.

[h] 1,3-Bis(4-(3-chlorophenyl)piperazin-1-yl)propane.

[i] 1,4-Bis(3-chlorophenyl)piperazine.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at controlled room temperature.

• **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Trazodone Hydrochloride RS

USP Trazodone Related Compound C RS

2-{3-[4-(4-Chlorophenyl)piperazin-1-yl]propyl}-[1,2,4]triazolo[4,3-*a*]pyridin-3(2*H*)-one hydrochloride.

$C_{19}H_{22}ClN_5O \cdot HCl$ ▲408.33▲ (USP 1-May-2023)

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

Topic/Question	Contact	Expert Committee
TRAZODONE HYDROCHLORIDE TABLETS	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. 47(5)

Current DocID: GUID-5BD7EA82-C83E-4EF2-AFEB-B31384EE744C_7_en-US

DOI: https://doi.org/10.31003/USPNF_M84492_07_01

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