Status: Currently Official on 15-Feb-2025
Official Date: Official as of 01-Aug-2023
Document Type: USP Monographs
DocId: GUID-A96DC592-6BD7-4D02-B302-B420CC161805_4_en-US
DOI: https://doi.org/10.31003/USPNF_M45930_04_01
DOI Ref: 721hv

Lorazepam Tablets

DEFINITION
Lorazepam Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of lorazepam ($C_{15}H_{10}Cl_2N_2O_2$).

IDENTIFICATION

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

Sample: Stir a portion of finely powdered Tablets, equivalent to 15 mg of lorazepam, with 40 mL of acetone for 5 min. Pass through very retentive filter paper pre-washed with acetone. Evaporate the filtrate to dryness on a steam bath with the aid of a current of air. Dissolve the residue in 1 mL of acetone, and add 20 mL of 2,2,4-trimethylpentane. Heat the solution on a hot plate to a gentle boil, and evaporate to a volume of about 10 mL. Remove the solution from the hot plate, and evaporate to dryness with the aid of a current of air. Dry the residue under vacuum at 60° for 1 h.

Acceptance criteria: Meet the requirements

• **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

• **Procedure**

Diluent: Methanol and water (85:15)

Mobile phase: Acetonitrile, glacial acetic acid, and water (40: 0.4: 60)

Standard solution: 0.1 mg/mL of USP Lorazepam RS in *Diluent*

Sample solution: Nominally 0.1 mg/mL of lorazepam prepared as follows. Transfer 20 Tablets to a 100-mL volumetric flask, add 50 mL of *Diluent*, sonicate for 10 min, and shake by mechanical means for 20 min. Dilute with *Diluent* to volume, mix, and centrifuge a portion of the solution at 2000 rpm for 10 min. Dilute a portion of the clear supernatant with *Diluent*.

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

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

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 lorazepam ($C_{15}H_{10}Cl_2N_2O_2$) in the portion of Tablets taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: Water; 500 mL

Apparatus 1: 100 rpm

Times: 30 and 60 min

Mobile phase and **Chromatographic system:** Prepare as directed in the *Assay*, except use an *Injection volume* of 50 µL.

Standard solution: USP Lorazepam RS at a known concentration in *Medium*. Initially, use a volume of alcohol not exceeding 10% of the final volume of the *Standard solution* to dissolve the Reference Standard.

Sample solution: Sample per *Dissolution ⟨711⟩*.

Analysis

Samples: *Standard solution* and *Sample solution*

Tolerances: NLT 60% (*Q*) of the labeled amount of lorazepam ($C_{15}H_{10}Cl_2N_2O_2$) is dissolved in 30 min. NLT 80% (*Q*) of the labeled amount of lorazepam ($C_{15}H_{10}Cl_2N_2O_2$) is dissolved in 60 min.

Change to read:

• **Uniformity of Dosage Units ⟨905⟩:** ▲Meet the requirements▲ (CN 1-Aug-2023)

Procedure for content uniformity

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

Sample solution: Nominally, 0.1 mg/mL of lorazepam prepared as follows. Place 1 Tablet in a volumetric flask of appropriate size, based on the labeled quantity, in mg, of lorazepam in the Tablet. Add a volume of *Diluent* equal to about 50% of the volume of the flask, sonicate for 10 min, and shake by mechanical means for 20 min. Dilute with *Diluent* to volume, mix, and centrifuge a portion of the solution for 10 min at 2000 rpm.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of lorazepam ($C_{15}H_{10}Cl_2N_2O_2$) in the portion of the Tablet taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

▲▲ (CN 1-Aug-2023)

IMPURITIES

• **Organic Impurities**

Buffer: 67.7 g/L of sodium acetate trihydrate in water. Adjust with glacial acetic acid to a pH of 5.0 ± 0.05.

Mobile phase: Acetonitrile, glacial acetic acid, and water (50: 1.2: 50)

Diluent: Methanol and *Buffer* (75:25)

Standard solution: 1.6 µg/mL of USP Lorazepam RS in *Diluent*

Peak identification solution: 0.16 mg/mL of USP Lorazepam RS, 1.6 µg/mL each of USP Lorazepam Related Compound A RS, USP Lorazepam Related Compound B RS, USP Lorazepam Related Compound C RS, USP Lorazepam Related Compound D RS, and USP Lorazepam Related Compound E RS in *Diluent*

Sample solution: Nominally 0.16 mg/mL of lorazepam prepared as follows. Transfer a weighed amount of lorazepam, equivalent to 21.3 mg from powdered Tablets, to a 25-mL volumetric flask. Add 20 mL of *Diluent*, and stir for 15 min. Do not dilute to volume. Centrifuge at 2000 rpm for 15 min. Pass the supernatant through a polyethersulfone membrane of 0.45-µm pore size. Dilute a portion of the filtrate with *Diluent*.

Chromatographic system

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

Mode: LC. Use an instrument equipped with a sample compartment chiller maintained at 4°.

Detector: UV 230 nm

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

Column temperature: 5°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: At least 50 min

System suitability

Samples: *Standard solution* and *Peak identification solution*

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

Suitability requirements

Resolution: NLT 1.2 between lorazepam related compound A and lorazepam related compound E, *Peak identification solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 5%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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

r_S = peak response for lorazepam from the *Standard solution*

C_S = concentration of lorazepam in the *Standard solution* (mg/mL)

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

F = relative response factor for any given impurity (see *Table 1*)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Lorazepam	1.0	1.0	—
Lorazepam related compound D[a]	1.4	1.0	0.5
Lorazepam related compound A[b,c]	1.7	—	—
Lorazepam related compound E[d]	1.9	1.3	0.5
Lorazepam related compound C[e]	2.1	1.0	3.0
Lorazepam related compound B[f]	5.5	1.0	0.1
Any individual unspecified degradation product	—	1.0	0.2
Total impurities	—	—	4.0

[a] 6-Chloro-4-(*o*-chlorophenyl)-2-quinazolinecarboxylic acid.

[b] 7-Chloro-5-(*o*-chlorophenyl)-1,3-dihydro-3-acetoxy-2*H*-1,4-benzodiazepin-2-one.

[c] Lorazepam related compound A is included only for peak identification purposes. It is not quantified and should not be included in the total impurities calculation.

[d] 6-Chloro-4-(*o*-chlorophenyl)-2-quinazoline methanol.

[e] 6-Chloro-4-(*o*-chlorophenyl)-2-quinazolinecarboxaldehyde.

[f] 2-Amino-2',5-dichlorobenzophenone.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers.
- **USP Reference Standards** ⟨11⟩

USP Lorazepam RS

USP Lorazepam Related Compound A RS

7-Chloro-5-(*o*-chlorophenyl)-1,3-dihydro-3-acetoxy-2*H*-1,4-benzodiazepin-2-one.

$C_{17}H_{12}Cl_2N_2O_3$ 363.20

USP Lorazepam Related Compound B RS

2-Amino-2',5-dichlorobenzophenone.

$C_{13}H_9Cl_2NO$ 266.12

USP Lorazepam Related Compound C RS

6-Chloro-4-(*o*-chlorophenyl)-2-quinazolinecarboxaldehyde.

$C_{15}H_8Cl_2N_2O$ 303.14

USP Lorazepam Related Compound D RS

6-Chloro-4-(*o*-chlorophenyl)-2-quinazolinecarboxylic acid.

$C_{15}H_8Cl_2N_2O_2$ 319.14

USP Lorazepam Related Compound E RS

6-Chloro-4-(*o*-chlorophenyl)-2-quinazoline methanol.

$C_{15}H_{10}Cl_2N_2O$ 305.16

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

Topic/Question	Contact	Expert Committee
LORAZEPAM TABLETS	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 33(3)

Current DocID: GUID-A96DC592-6BD7-4D02-B302-B420CC161805_4_en-US

DOI: https://doi.org/10.31003/USPNF_M45930_04_01

DOI ref: 721hv