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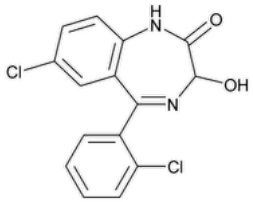
Lorazepam



$C_{15}H_{10}Cl_2N_2O_2$ 321.16

2*H*-1,4-Benzodiazepin-2-one, 7-chloro-5-(2-chlorophenyl)-1,3-dihydro-3-hydroxy-, (±)-;

(±)-7-Chloro-5-(*o*-chlorophenyl)-1,3-dihydro-3-hydroxy-2*H*-1,4-benzodiazepin-2-one CAS RN®: 846-49-1; UNII: O26FZP769L.

DEFINITION

Lorazepam contains NLT 98.0% and NMT 102.0% of lorazepam ($C_{15}H_{10}Cl_2N_2O_2$), calculated on the dried basis.

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A or 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*.

ASSAY

Change to read:

- **Procedure**

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

Diluent: Methanol and water (75:25)

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

Sample solution: 0.1 mg/mL of Lorazepam in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

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

Temperatures

▲Autosampler:▲ (USP 1-Dec-2021) 4°

Column: 5°

Flow rate: 1 mL/min

Injection volume: 5 µL

▲Run time: NLT 8 times the retention time of lorazepam▲ (USP 1-Dec-2021)

System suitability

Sample: *Standard solution*

▲▲ (USP 1-Dec-2021)

Suitability requirements

Tailing factor: NMT ▲1.5▲ (USP 1-Dec-2021)

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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

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

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

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

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

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.3%

Change to read:

• **Organic Impurities**

Mobile phase and **Diluent:** Prepare as directed in the *Assay*.

System suitability solution: 3.2 mg/mL of USP Lorazepam RS and 32 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*

▲**Sensitivity solution:** 0.16 µg/mL of USP Lorazepam Related Compound B RS in *Diluent*▲ (USP 1-Dec-2021)

Standard solution: ▲3.2▲ (USP 1-Dec-2021) µg/mL of USP Lorazepam RS in *Diluent*

Sample solution: 3.2 mg/mL of Lorazepam in *Diluent*

Chromatographic system: ▲Proceed as directed in the *Assay*, except for *Injection volume*.▲ (USP 1-Dec-2021)

Injection volume: 100 µL

System suitability

Samples: *System suitability solution*, ▲*Sensitivity solution*,▲ (USP 1-Dec-2021) and *Standard solution*

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

▲▲ (USP 1-Dec-2021)

Suitability requirements

Resolution: NLT 1.2 between lorazepam related compound A and lorazepam related compound E, *System suitability solution*

▲▲ (USP 1-Dec-2021)

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

▲**Signal-to-noise ratio:** NLT 10 for lorazepam related compound B, *Sensitivity solution*▲ (USP 1-Dec-2021)

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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

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

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

C_U = 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	1.4	1.0	0.15
Lorazepam related compound A	1.7	1.0	0.10

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Lorazepam related compound E	1.9	1.3	0.15
Lorazepam related compound C	2.1	1.0	0.30
Lorazepam related compound B	5.5	1.0	0.01
Any individual unspecified impurity	—	1.0	0.10
Total impurities	—	—	0.75

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

Analysis: Dry under vacuum at 105° for 3 h.

Acceptance criteria: NMT 0.5%

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	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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