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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*