Status: Currently Official on 15-Feb-2025
Official Date: Official as of 01-Aug-2017
Document Type: USP Monographs
DocId: GUID-822437DA-3092-475C-B617-27EDE904AE3F_1_en-US
DOI: https://doi.org/10.31003/USPNF_M45920_01_01
DOI Ref: u22s5

Lorazepam Oral Concentrate

DEFINITION

Lorazepam Oral Concentrate contains NLT 90.0% and NMT 110.0% of the labeled amount of lorazepam ($C_{15}H_{10}Cl_2N_2O_2$).

IDENTIFICATION

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

ASSAY

- **Procedure**

Mobile phase: Acetonitrile, glacial acetic acid, and water (45:0.2:55)

System suitability solution: 0.1 mg/mL each of USP Lorazepam RS and USP Lorazepam Related Compound E RS in methanol

Standard solution: 0.05 mg/mL of USP Lorazepam RS in methanol

Sample solution: Nominally 0.05 mg/mL of lorazepam prepared as follows. Transfer a suitable volume of Oral Concentrate to a volumetric flask, and dilute with methanol to volume.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm. For *Identification B*, use a diode-array detector in the range of 220–400 nm.

Column: 4-mm × 30-cm; packing L1

Flow rate: 2 mL/min

Injection volume: 20 µL

System suitability

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

[Note—The relative retention times for lorazepam and lorazepam related compound E are 0.6 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between lorazepam and lorazepam related compound E, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

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 Oral Concentrate 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%

IMPURITIES

- **Organic Impurities**

Mobile phase: Methanol and 0.05 M monobasic ammonium phosphate (64:36)

Diluent: Methanol and 0.05 M monobasic ammonium phosphate (50:50). Adjust with ammonium hydroxide to a pH of 6.5.

System suitability solution: 0.04 mg/mL of USP Lorazepam RS, and 0.032 mg/mL each of USP Lorazepam Related Compound C RS and USP Lorazepam Related Compound D RS in *Diluent*

Standard stock solution: 1.0 mg/mL of USP Lorazepam RS in methanol

Standard solution 1: 0.16 µg/mL of lorazepam from the *Standard stock solution* in *Diluent*

Standard solution 2: 0.16 µg/mL of USP Lorazepam Related Compound B RS, and 3.2 µg/mL each of USP Lorazepam Related Compound C RS and USP Lorazepam Related Compound D RS in *Mobile phase*

Sample solution: Nominally 0.16 mg/mL of lorazepam prepared as follows. Transfer a suitable volume of Oral Concentrate to a volumetric flask, and dilute with *Mobile phase* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

Column: 4.6-mm × 10- to 15-cm; packing L1

Flow rate: 0.7 mL/min

Injection volume: 20 µL

System suitability

Samples: *System suitability solution* and *Standard solution 1*

Suitability requirements

Resolution: NLT 1.2 between lorazepam related compound D and lorazepam; NLT 1.2 between lorazepam and lorazepam related compound C, *System suitability solution*

Relative standard deviation: NMT 2.0% for lorazepam, *Standard solution 1*

Analysis

Samples: *Standard solution 2* and *Sample solution*

[NOTE—Disregard peaks eluting prior to lorazepam related compound D.]

Calculate the percentage of lorazepam related compound B, lorazepam related compound C, and lorazepam related compound D in the portion of Oral Concentrate taken:

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

r_U = peak response of lorazepam related compound B, lorazepam related compound C, or lorazepam related compound D from the *Sample solution*

r_S = peak response of the corresponding related compound from *Standard solution 2*

C_S = concentration of the corresponding related compound in *Standard solution 2* (mg/mL)

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

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Lorazepam related compound D	0.8	4.0[a]
Lorazepam	1.0	—
Lorazepam related compound C	2.3	4.0[a]
Lorazepam related compound B	2.9	0.1

[a] Includes the sum of lorazepam related compound C and lorazepam related compound D.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed, light-resistant containers, and store in a refrigerator.
- **USP Reference Standards** ⟨11⟩

USP Lorazepam RS

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 ORAL CONCENTRATE	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. PF 42(3)

Current DocID: GUID-822437DA-3092-475C-B617-27EDE904AE3F_1_en-US

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