Status: Currently Official on 15-Feb-2025
Official Date: Official as of 01-May-2018
Document Type: USP Monographs
DocId: GUID-DC4075C3-13A4-46B2-919D-B8A04D55CEB5_3_en-US
DOI: https://doi.org/10.31003/USPNF_M45915_03_01
DOI Ref: 46zoz

Lorazepam Injection

DEFINITION

Lorazepam Injection is a sterile solution of Lorazepam in a suitable medium. It 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**

Buffer: 0.05 M monobasic ammonium phosphate

Mobile phase: Methanol and *Buffer* (50:50). Adjust with ammonium hydroxide to a pH of 6.5.

System suitability solution: 0.04 mg/mL of lorazepam and 32 µg/mL each of USP Lorazepam Related Compound C RS and USP Lorazepam Related Compound D RS in *Mobile phase*

Standard stock solution: 1 mg/mL of USP Lorazepam RS in methanol

Standard solution: 0.16 mg/mL of USP Lorazepam RS in *Mobile phase* from the *Standard stock solution*

Sample solution: Nominally 0.16 mg/mL of lorazepam from Injection, diluted with *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 240 nm. For *Identification B*, use a diode array detector in the range of 210–400 nm.

Column: 4.6-mm × 10 to 15-cm; 5-µm packing L1

Flow rate: 2 mL/min

Injection volume: 20 µL

Run time: NLT 3 times the retention time of lorazepam

System suitability

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

[Note—The relative retention times for lorazepam related compound D, lorazepam, and lorazepam related compound C are 0.7, 1.0, and 2.7, respectively.]

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%, *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 Injection 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 = nominal concentration of lorazepam in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

IMPURITIES

- **Organic Impurities**

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

Standard solution 1: Prepare as directed for the *Standard solution* in the *Assay*.

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

System suitability

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

[Note—The relative retention times for lorazepam related compound D, lorazepam, and lorazepam related compound C are 0.7, 1.0, and 2.7, respectively.]

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%, *Standard solution 1*

Analysis

Samples: *Sample solution* and *Standard solution 2*. Do not include as an impurity any peak from the *Sample solution* that has a retention time shorter than that of the lorazepam related compound D peak from *Standard solution 2*.

Calculate the percentage of lorazepam related compound C and lorazepam related compound D in the portion of Injection taken:

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

r_U = peak response of 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* (µg/mL)

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

Calculate the percentage of any other impurity in the portion of Injection taken:

$$\text{Result} = (r_U/r_T) \times 100$$

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

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

Acceptance criteria: NMT 4.0% of all impurities

- **Limit of Lorazepam Related Compound B**

Buffer: 0.05 M monobasic ammonium phosphate. Adjust with ammonium hydroxide to a pH of 6.5.

Mobile phase: Methanol and *Buffer* (55:45)

Diluent: Methanol and *Buffer* (50:50)

Standard solution: 0.16 µg/mL of USP Lorazepam Related Compound B RS in *Diluent*. Sonicate to dissolve if necessary.

Sample solution: Nominally 0.16 mg/mL of lorazepam from Injection, diluted with *Diluent*. Sonicate to dissolve if necessary.

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

Column: 4.6-mm × 10-cm; 5-µm packing L1

Flow rate: 2 mL/min

Injection volume: 50 µL

Run time: 1.5 times the retention time of lorazepam related compound B

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 5.0%

Signal-to-noise ratio: NLT 10

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of lorazepam related compound B in the portion of Injection taken:

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

r_U = peak response of lorazepam related compound B from the *Sample solution*

r_S = peak response of lorazepam related compound B from the *Standard solution*

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

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

Acceptance criteria: NMT 0.1%

SPECIFIC TESTS

• **Bacterial Endotoxins Test ⟨85⟩:** Contains NMT 10^2 USP Endotoxin Units/mg of lorazepam

• **Other Requirements:** It meets the requirements in *Injections and Implanted Drug Products ⟨1⟩*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in single-dose or multiple-dose containers, preferably of Type I glass, protected from light. 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

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

Topic/Question	Contact	Expert Committee
LORAZEPAM INJECTION	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(6)

Current DocID: GUID-DC4075C3-13A4-46B2-919D-B8A04D55CEB5_3_en-US
Previous DocID: GUID-DC4075C3-13A4-46B2-919D-B8A04D55CEB5_1_en-US
DOI: https://doi.org/10.31003/USPNF_M45915_03_01
DOI ref: 46zoz