Status: Currently Official on 15-Feb-2025
Official Date: Official as of 01-Aug-2022
Document Type: USP Monographs
DocId: GUID-A829256D-260B-4325-84E1-65F38D4BCEA3_2_en-US
DOI: https://doi.org/10.31003/USPNF_M46040_02_01
DOI Ref: olz7a

Loxapine Capsules

DEFINITION

Loxapine Capsules contain an amount of loxapine succinate ($C_{18}H_{18}ClN_3O \cdot C_4H_6O_4$) equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of loxapine ($C_{18}H_{18}ClN_3O$).

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*.

Add the following:

▲• **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-Aug-2022)

ASSAY

Change to read:

• **Procedure**

Mobile phase: Dissolve 4 g of tetramethylammonium chloride in 800 mL of water, and add 200 mL of acetonitrile and 1 mL of phosphoric acid.

Standard solution: 0.136 mg/mL of USP Loxapine Succinate RS prepared as follows. Dissolve a suitable quantity of USP Loxapine Succinate RS in 0.01 N hydrochloric acid in a suitable volumetric flask, and dilute with *Mobile phase* to volume.

Sample solution: Nominally 0.1 mg/mL of loxapine prepared as follows. Weigh the contents of Capsules (NLT 20). Transfer a portion of the contents, nominally equivalent to NLT 50 mg of loxapine, to a suitable volumetric flask. Add 10% of the flask volume of 0.1 N hydrochloric acid. Shake, and sonicate for 5 min. Dilute with *Mobile phase* to volume, and filter. Discard the first 8 mL of the filtrate.

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.▲ (USP 1-Aug-2022)

Column: 4.6-mm × 15-cm; 5-µm packing L10

Flow rate: 1.6 mL/min

Injection volume: 20 µL

▲**Run time:** NLT 4 times the retention time of loxapine▲ (USP 1-Aug-2022)

System suitability

Sample: *Standard solution*

Suitability requirements

▲▲ (USP 1-Aug-2022)

Tailing factor: NMT 2.0

Relative standard deviation: NMT ▲1.0%▲ (USP 1-Aug-2022)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of loxapine ($C_{18}H_{18}ClN_3O$) in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak ▲response of loxapine▲ (USP 1-Aug-2022) from the *Sample solution*

r_S = peak ▲response of loxapine▲ (USP 1-Aug-2022) from the *Standard solution*

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

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

M_{r1} = molecular weight of loxapine, 327.81

M_{r2} = molecular weight of loxapine succinate, 445.90

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Medium: Water; 900 mL

Apparatus 1: 100 rpm

Time: 45 min

Standard solution: USP Loxapine Succinate RS at a known concentration in *Medium*

Sample solution: Dilute with water as needed.

Instrumental conditions

▲(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)▲ (USP 1-Aug-2022)

Mode: UV

Analytical wavelength: 254 nm

Analysis

Samples: *Standard solution* and *Sample solution*

▲Calculate the percentage of the labeled amount of loxapine ($C_{18}H_{18}ClN_3O$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times (M_{r1}/M_{r2}) \times V \times D \times (1/L) \times 100$$

A_U = absorbance of loxapine from the *Sample solution*

A_S = absorbance of loxapine from the *Standard solution*

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

M_{r1} = molecular weight of loxapine, 327.81

M_{r2} = molecular weight of loxapine succinate, 445.90

V = volume of *Medium*, 900 mL

D = dilution factor of the *Sample solution*

L = label claim (mg/Capsule)▲ (USP 1-Aug-2022)

Tolerances: NLT 75% (Q) of the labeled amount of loxapine ($C_{18}H_{18}ClN_3O$) is dissolved.

• **Uniformity of Dosage Units** ⟨905⟩**:** Meet the requirements

Add the following:

▲IMPURITIES

• **Organic Impurities**

Buffer: 3.9 g/L of ammonium acetate in water. Adjust with 20% acetic acid or 6 N ammonium hydroxide to a pH of 7.3.

Solution A: *Buffer*

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	70	30
1	70	30
18	20	80
20	20	80
21	70	30
25	70	30

Diluent: Acetonitrile and *Buffer* (70:30)

System suitability solution: 0.3 mg/mL of USP Loxapine Succinate RS and 0.45 µg/mL of USP Loxapine Related Compound A RS in *Diluent*

Standard solution: 0.3 µg/mL each of USP Loxapine Succinate RS and USP Loxapine *N*-Oxide RS in *Diluent*

Sample solution: Nominally 0.22 mg/mL of loxapine prepared as follows. Weigh and mix the contents of Capsules (NLT 10). Transfer a portion of the contents, nominally equivalent to 22 mg of loxapine, to a 100-mL volumetric flask. Add 70% of the flask volume of *Diluent*. Shake, and sonicate for 5 min. Dilute with *Diluent* to volume, and filter.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 10-cm; 2.7-µm packing L1

Column temperature: 35°

Flow rate: 1.4 mL/min

Injection volume: 10 µL

System suitability

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

[NOTE—See *Table 2* for the relative retention times. The relative retention times for amoxapine and loxapine related compound A are 0.46 and 1.03, respectively.]

Suitability requirements

Resolution: NLT 2.0 between loxapine and loxapine related compound A, *System suitability solution*

Relative standard deviation: NMT 5.0% for loxapine and loxapine *N*-oxide, *Standard solution*

Signal-to-noise ratio: NLT 10 for loxapine *N*-oxide, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of loxapine *N*-oxide in the portion of Capsules taken:

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

r_U = peak response of loxapine *N*-oxide from the *Sample solution*

r_S = peak response of loxapine *N*-oxide from the *Standard solution*

C_S = concentration of USP Loxapine *N*-Oxide RS in the *Standard solution* (mg/mL)

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

Calculate the percentage of any other individual degradation product in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 1/F \times 100$$

r_U = peak response of any other individual degradation product from the *Sample solution*

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

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

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

M_{r1} = molecular weight of loxapine, 327.81

M_{r2} = molecular weight of loxapine succinate, 445.90

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*. The reporting threshold is 0.1%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Loxapine *N*-oxide	0.39	—	0.2
Amoxapine related compound D[a]	0.73	0.70	0.2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Loxapine succinate	1.0	—	—
Any unspecified degradation product	—	1.0	0.2
Total degradation products	—	—	1.0

[a] 2-Chlorodibenzo[*b*,*f*]-1,4-oxazepin-11-one.

▲ (USP 1-Aug-2022)

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in tight containers. ▲Store at controlled room temperature.▲ (USP 1-Aug-2022)

Change to read:

• **USP Reference Standards** (11)

USP Loxapine Succinate RS

▲ USP Loxapine *N*-Oxide RS

4-(2-Chlorodibenzo[*b*,*f*][1,4]oxazepin-11-yl)-1-methylpiperazine 1-oxide.

$C_{18}H_{18}ClN_3O_2$ 343.81

USP Loxapine Related Compound A RS

3-Chloro-11-(4-methylpiperazin-1-yl)dibenzo[*b*,*f*][1,4]oxazepine.

$C_{18}H_{18}ClN_3O$ 327.81▲ (USP 1-Aug-2022)

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

Topic/Question	Contact	Expert Committee
LOXAPINE CAPSULES	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 46(6)

Current DocID: GUID-A829256D-260B-4325-84E1-65F38D4BCEA3_2_en-US

DOI: https://doi.org/10.31003/USPNF_M46040_02_01

DOI ref: olz7a