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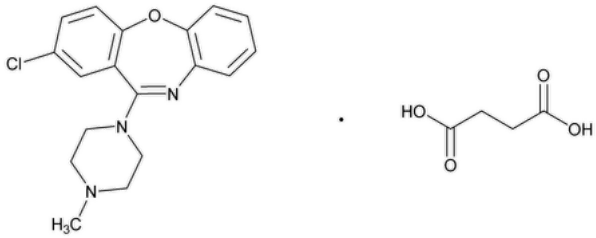
Loxapine Succinate



$C_{18}H_{18}ClN_3O \cdot C_4H_6O_4$ 445.90

Butanedioic acid, compd. with 2-chloro-11-(4-methyl-1-piperazinyl)dibenz[*b*,*f*][1,4]oxazepine (1:1);

2-Chloro-11-(4-methyl-1-piperazinyl)dibenz[*b*,*f*][1,4]oxazepine succinate (1:1) CAS RN®: 27833-64-3; UNII: X59SG0MRYU.

Change to read:

DEFINITION

Loxapine Succinate contains NLT ▲98.0%▲ (USP 1-Aug-2022) and NMT ▲102.0%▲ (USP 1-Aug-2022) of loxapine succinate ($C_{18}H_{18}ClN_3O \cdot C_4H_6O_4$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K ▲or 197A▲ (USP 1-Aug-2022)

Delete the following:

▲• **B. Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*:** 197U

Sample solution: 20 µg/mL in 0.01 N hydrochloric acid▲ (USP 1-Aug-2022)

Add the following:

▲• **B.** The retention time 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**

▲**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

Time (min)	Solution A (%)	Solution B (%)
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 mg/mL of USP Loxapine Succinate RS in *Diluent*

Sample solution: 0.3 mg/mL of Loxapine Succinate in *Diluent*

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.]

Suitability requirements

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

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of loxapine succinate ($C_{18}H_{18}ClN_3O \cdot C_4H_6O_4$) in the portion of Loxapine Succinate taken:

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

r_U = peak response of loxapine 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 = concentration of Loxapine Succinate in the *Sample solution* (mg/mL)▲ (USP 1-Aug-2022)

Acceptance criteria: ▲98.0%–102.0%▲ (USP 1-Aug-2022) on the dried basis

IMPURITIES

• **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.1%

Change to read:

• **ORGANIC IMPURITIES**

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

Standard solution: 0.3 µg/mL each of USP Loxapine Succinate RS and USP Loxapine *N*-Oxide RS in *Diluent*▲ (USP 1-Aug-2022)

System suitability

Samples: ▲*System suitability solution* and▲ (USP 1-Aug-2022) *Standard solution*

▲[NOTE—See *Table 2* for the relative retention times.]▲ (USP 1-AUG-2022)

Suitability requirements

Resolution: NLT 2.0 between loxapine ▲▲ (USP 1-Aug-2022) and loxapine related compound A, ▲*System suitability solution*▲ (USP 1-Aug-2022)

Relative standard deviation: NMT 5.0% ▲for loxapine *N*-oxide and loxapine,▲ (USP 1-Aug-2022) *Standard solution*

▲**Signal-to-noise ratio:** NLT 10 for loxapine *N*-oxide, *Standard solution*▲ (USP 1-Aug-2022)

Analysis

Samples: *Standard solution* and *Sample solution*

▲Calculate the percentage of loxapine *N*-oxide in the portion of Loxapine Succinate 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 = concentration of Loxapine Succinate in the *Sample solution* (mg/mL)▲ (USP 1-Aug-2022)

Calculate the percentage of any ▲other▲ (USP 1-Aug-2022) individual impurity in the portion of Loxapine Succinate taken:

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

r_U = peak response of each ▲other▲ (USP 1-Aug-2022) impurity 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 = concentration of Loxapine Succinate in the *Sample solution* (mg/mL)

F = relative response factor (see ▲*Table 2*▲ (USP 1-Aug-2022))

Acceptance criteria: ▲See *Table 2*. The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Loxapine *N*-oxide	0.39	—	0.10
Amoxapine[a]	0.46	1.4	0.15
Amoxapine related compound D[b]	0.72	0.70	0.15
Loxapine	1.0	—	—
Loxapine related compound A	1.03	1.7	0.15
Any unspecified impurity	—	1.0	0.10
Total impurities	—	—	0.5▲ (USP 1-Aug-2022)

[a] 2-Chloro-11-(piperazin-1-yl)dibenzo[*b*,*f*][1,4]oxazepine.

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

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

Analysis: Dry at 105° for 4 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.

Change to read:

• **USP Reference Standards** ⟨11⟩

▲▲ (USP 1-Aug-2022)

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 1-Aug-2022)

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

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

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

Chromatographic Database Information: Chromatographic Database

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