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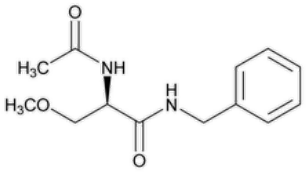
Add the following:

▲Lacosamide



$C_{13}H_{18}N_2O_3$ 250.30

Propanamide, 2-(acetylamino)-3-methoxy-*N*-(phenylmethyl)-, (2*R*)-;

(+)-(*R*)-2-(Acetylamino)-*N*-benzyl-3-methoxypropanamide. CAS RN®: 175481-36-4.

DEFINITION

Lacosamide contains NLT 98.0% and NMT 102.0% of lacosamide ($C_{13}H_{18}N_2O_3$).

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K or 197A

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *System suitability solution*, as obtained in the test for *Limit of Lacosamide S-Enantiomer*.

ASSAY

• **Procedure**

Solution A: To each liter of water add 1 mL of trifluoroacetic acid.

Solution B: Acetonitrile and methanol (50:50). To each liter add 0.3 mL of trifluoroacetic acid.

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	89	11
12.2	69	31
17.5	23	77
18.0	0	100
19.0	0	100
19.1	89	11
24.0	89	11

System suitability solution: 5 mg/mL of USP Lacosamide RS and 10 µg/mL each of USP Lacosamide Related Compound B RS and *N*-benzylacetamide prepared as follows. Weigh an appropriate amount of USP Lacosamide RS, USP Lacosamide Related Compound B RS, and *N*-benzylacetamide into a suitable volumetric flask. Dissolve in 10% of the flask volume of methanol. Dilute with water to volume.

Standard solution: 5 mg/mL of USP Lacosamide RS prepared as follows. Weigh an appropriate amount of USP Lacosamide RS into a suitable volumetric flask. Dissolve in 10% of the flask volume of methanol. Dilute with water to volume.

Sample solution: 5 mg/mL of Lacosamide prepared as follows. Weigh an appropriate amount of Lacosamide into a suitable volumetric flask. Dissolve in 10% of the flask volume of methanol. Dilute with water to volume.

Chromatographic system

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

Mode: LC

Detector: UV 258 nm

Column: 4.6-mm × 15-cm; 3.5-µm packing L7

Autosampler temperature: 10°

Flow rate: 1.2 mL/min

Injection volume: 20 µL

System suitability

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

[NOTE—See *Table 2* for relative retention times.]

Suitability requirements

Resolution: NLT 2.0 between *N*-benzylacetamide and lacosamide; NLT 4.5 between lacosamide and lacosamide related compound B, *System suitability solution*

Tailing factor: NMT 2.5, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of lacosamide ($C_{13}H_{18}N_2O_3$) in the portion of Lacosamide 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 the USP Lacosamide RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 98.0%–102.0%

IMPURITIES

- **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.1%
- **LIMIT OF LACOSAMIDE *S*-ENANTIOMER**

Mobile phase: Heptane, isopropyl alcohol, and water (90: 10: 0.3)

System suitability solution: 1 mg/mL of USP Lacosamide RS and 5 µg/mL of USP Lacosamide *S*-Enantiomer RS in *Mobile phase*

Sample solution: 1 mg/mL of Lacosamide in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 25-cm; 10-µm packing L51

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 1.7 times the retention time of lacosamide

System suitability

Sample: *System suitability solution*

[NOTE—The relative retention times for lacosamide *S*-enantiomer and lacosamide are 0.75 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 3.0 between lacosamide *S*-enantiomer and lacosamide

Signal-to-noise ratio: NLT 10 for *S*-enantiomer

Analysis

Sample: *Sample solution*

Calculate the percentage of *S*-enantiomer in the portion of Lacosamide taken:

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

r_U = peak response of *S*-enantiomer

r_T = sum of the peak responses of lacosamide and *S*-enantiomer

Acceptance criteria: NMT 0.15%

- **Organic Impurities**

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

Diluent: Methanol and water (10:90)

Sensitivity solution: 2.5 µg/mL of USP Lacosamide RS in *Diluent*

Standard solution: 0.005 mg/mL of USP Lacosamide RS in *Diluent*

System suitability

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

[Note—See *Table 2* for relative retention times.]

Suitability requirements

Resolution: NLT 2.0 between *N*-benzylacetamide and lacosamide; NLT 4.5 between lacosamide and lacosamide related compound B, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of each impurity in the portion of Lacosamide taken:

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

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

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

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

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

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

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

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Lacosamide related compound F[a]	0.68	1.0	0.15
N-Benzylacetamide	0.92	1.4	0.15
Lacosamide	1.0	1.0	—
Lacosamide related compound B	1.15	1.0	0.15
N-Methyl lacosamide[b]	1.32	1.0	0.15

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Ureidolacosamide[c]	1.53	1.4	0.15
Any individual unspecified impurity	—	1.0	0.10
Total impurities	—	—	0.5

[a] 2-Acetamido-*N*-benzyl-3-hydroxypropanamide.

[b] (*R*)-*N*-Benzyl-3-methoxy-2-(*N*-methylacetamido)propanamide.

[c] (*R*)-*N*-Benzyl-2-(3-benzylureido)-3-methoxypropanamide.

SPECIFIC TESTS

• **Water Determination ⟨921⟩, *Method I*:** NMT 0.2%. [Note—*Method Ia* or *Method Ic* may be used.]

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers, and store at controlled room temperature.

• **USP Reference Standards ⟨11⟩**

USP Lacosamide RS

USP Lacosamide Related Compound B RS

2-Acetamido-3-(benzylamino)-3-oxopropyl acetate.

$C_{14}H_{18}N_2O_4$ 278.31

USP Lacosamide *S*-Enantiomer RS

(*S*)-2-(Acetylamino)-*N*-benzyl-3-methoxypropanamide.

$C_{13}H_{18}N_2O_3$ 250.29▲ (USP 1-May-2021)

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

Topic/Question	Contact	Expert Committee
LACOSAMIDE	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

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