## Lacosamide Oral Solution

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| **Type of Posting** | Notice of Intent to Revise |
| **Posting Date** | 25-Feb-2022 |
| **Targeted Official Date** | To Be Determined, Revision Bulletin |
| **Expert Committee** | Small Molecules 4 |

In accordance with the Rules and Procedures of the Council of Experts and the Pending Monograph Guideline, this is to provide notice that the Small Molecules 4 Expert Committee intends to revise the Lacosamide Oral Solution monograph.

Based on the supporting data received from a manufacturer awaiting FDA approval, the Expert Committee proposes to widen the acceptance criteria for the *pH* test from 3.8–5.0 to 3.8–6.0 to accommodate drug products with wider acceptance criteria.

The proposed revision is contingent on FDA approval of a product that meets the proposed monograph specifications. The proposed revision will be published as a Revision Bulletin and an official date will be assigned to coincide as closely as possible with the FDA approval of the associated product.

See below for additional information about the proposed text.[1]

Should you have any questions, please contact Claire Chisolm, Senior Scientist II (301-230-3215 or cnc@usp.org).

[1] This text is not the official version of a *USP–NF* monograph and may not reflect the full and accurate contents of the currently official monograph. Please refer to the current edition of the *USP–NF* for official text.

USP provides this text to indicate changes that we anticipate will be made official once the product subject to this proposed revision under the Pending Monograph Program receives FDA approval. Once FDA approval is granted for the associated revision request, a Revision Bulletin will be posted that will include the changes indicated herein, as well as any changes indicated in the product's final approval, combined with the text of the monograph as effective on the date of approval. Any revisions made to a monograph under the Pending Monograph Program that are posted without prior publication for comment in the *Pharmacopeial Forum* must also meet the requirements outlined in the USP Guideline on Use of Accelerated Processes for Revisions to the *USP–NF*.

No Editorial Corrections

# Lacosamide Oral Solution

## DEFINITION

Lacosamide Oral Solution contains NLT 90.0% and NMT 105.0% of the labeled amount of lacosamide ($C_{13}H_{18}N_2O_3$).

## IDENTIFICATION

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

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

## ASSAY

● **Procedure**

**Solution A:** To each liter of water add 0.5 mL of trifluoroacetic acid.

**Solution B:** To each liter of acetonitrile add 0.5 mL of trifluoroacetic acid.

**Mobile phase:** See *Table 1*.

**Table 1**

| Time (min) | Solution A (%) | Solution B (%) |
|---|---|---|
| 0 | 75 | 25 |
| 9 | 75 | 25 |
| 9.01 | 45 | 55 |
| 12.50 | 45 | 55 |
| 12.51 | 75 | 25 |
| 16.00 | 75 | 25 |

**Diluent:** Acetonitrile and water (25:75)

**Standard solution:** 1.0 mg/mL of USP Lacosamide RS in *Diluent*

**Sample solution:** Nominally 1.0 mg/mL of lacosamide from Oral Solution prepared as follows. Transfer a volume of Oral Solution to a suitable volumetric flask. Dilute with *Diluent* to volume.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 215 nm. For *Identification A*, use a diode array detector in the range of 230–300 nm.

**Column:** 4.6-mm × 25-cm; 5-µm packing L1

**Temperatures:**

**Autosampler:** 10°

**Column:** 30°

**Flow rate:** 1.5 mL/min

**Injection volume:** 4 µL

**System suitability**

**Sample:** *Standard solution*

**Suitability requirements**

**Tailing factor:** NMT 1.5

**Relative standard deviation:** NMT 1.0%

**Analysis**

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

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

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

**Acceptance criteria:** 90.0%–105.0%

## PERFORMANCE TESTS

- **Deliverable Volume** ⟨698⟩**:** Meets the requirements

## IMPURITIES

- **Organic Impurities**

**Solution A:** Acetonitrile and water (10:90). To each liter add 0.56 mL of trifluoroacetic acid.

**Solution B:** To each liter of acetonitrile add 0.5 mL of trifluoroacetic acid.

**Mobile phase:** See *Table 2*.

**Table 2**

| Time (min) | Solution A (%) | Solution B (%) |
|---|---|---|
| 0 | 100 | 0 |
| 31.00 | 100 | 0 |
| 31.01 | 30 | 70 |
| 33.00 | 30 | 70 |
| 33.01 | 100 | 0 |

| Time (min) | Solution A (%) | Solution B (%) |
|---|---|---|
| 38.50 | 100 | 0 |

**Diluent:** Acetonitrile and water (25:75)

**System suitability solution:** 1 mg/mL of USP Lacosamide RS and 0.002 mg/mL each of USP Lacosamide Related Compound D RS and USP Lacosamide Related Compound F RS in *Diluent*

**Sensitivity solution:** 0.001 mg/mL of USP Lacosamide RS in *Diluent*

**Standard solution:** 0.002 mg/mL of USP Lacosamide RS in *Diluent*

**Sample solution:** Prepare as directed in the *Assay*.

**Chromatographic system:** Proceed as directed in the *Assay*, except for the *Injection volume*.

**Injection volume:** 5 µL

**System suitability**

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

[NOTE—The relative retention times for lacosamide related compound D, lacosamide related compound F, and lacosamide are 0.36, 0.48, and 1.0, respectively.]

**Suitability requirements**

**Resolution:** NLT 3.0 between lacosamide related compound D and lacosamide related compound F, *System suitability solution*

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

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

**Analysis**

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

Calculate the percentage of each degradation product in the portion of Oral Solution taken:

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

$r_U$ = peak response of each degradation product 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)

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

**Acceptance criteria:** The reporting threshold is 0.1%.

**Lacosamide related compound D:** NMT 0.80%

**Any individual unspecified degradation product:** NMT 0.20%

**Total degradation products:** NMT 2.0%

**SPECIFIC TESTS**

● **MICROBIAL ENUMERATION TESTS** ⟨61⟩ and **TESTS FOR SPECIFIED MICROORGANISMS** ⟨62⟩**:** The total aerobic microbial count does not exceed $10^2$ cfu/mL. The total yeasts and molds count does not exceed $10^1$ cfu/mL. It meets the requirements of the test for absence of *Escherichia coli*.

***Change to read:***

● **pH** ⟨791⟩**:** 3.8–▲6.0▲ (TBD)

## ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in light-resistant containers. Store at controlled room temperature.
- **USP Reference Standards** ⟨11⟩

  USP Lacosamide RS

  USP Lacosamide Related Compound D RS

  2-Amino-*N*-benzyl-3-methoxypropanamide oxalate.

  $C_{11}H_{16}N_2O_2 \cdot C_2H_2O_4$ 298.30

  USP Lacosamide Related Compound F RS

  2-Acetamido-*N*-benzyl-3-hydroxypropanamide.

  $C_{12}H_{16}N_2O_3$ 236.27

**Page Information:**

Not Applicable

**Current DocID:**