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# Levetiracetam Oral Solution

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click https://www.uspnf.com/rb-levetiracetam-oral-solution-20191122.

## DEFINITION

Levetiracetam Oral Solution contains NLT 90.0% and NMT 110.0% of the labeled amount of levetiracetam ($C_8H_{14}N_2O_2$).

## IDENTIFICATION

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

## ASSAY

• **Procedure**

**Solution A:** Dilute 1 mL of phosphoric acid with water to 1 L.

**Solution B:** Acetonitrile

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

**Table 1**

| Time (min) | Solution A (%) | Solution B (%) |
|---|---|---|
| 0 | 92 | 8 |
| 6 | 92 | 8 |
| 7 | 40 | 60 |
| 10 | 40 | 60 |
| 11 | 92 | 8 |
| 15 | 92 | 8 |

**Standard solution:** 1.0 mg/mL of USP Levetiracetam RS in *Solution A*

**Sample solution:** Nominally 1.0 mg/mL of levetiracetam prepared as follows. Transfer a suitable volume of the Oral Solution to a suitable volumetric flask to obtain 1.0 mg/mL final concentration of levetiracetam. Add 60% of the flask volume of *Solution A*, and sonicate at room temperature for 5 min with intermittent shaking. Allow the solution to cool, and dilute with *Solution A* to volume. Pass a portion of the solution under test through a suitable filter.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 230 nm

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

**Flow rate:** 1.5 mL/min

**Injection volume:** 20 µL

**System suitability**

**Sample:** *Standard solution*

**Suitability requirements**

**Tailing factor:** NMT 2.0

**Relative standard deviation:** NMT 2.0%

**Analysis**

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

Calculate the percentage of the labeled amount of levetiracetam ($C_8H_{14}N_2O_2$) 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 levetiracetam from the *Sample solution*

$r_S$ = peak response of levetiracetam from the *Standard solution*

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

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

**Acceptance criteria:** 90.0%–110.0%

## IMPURITIES

• **Organic Impurities**

**Solution A:** Dilute 2 mL of phosphoric acid with water to 1 L.

**Solution B:** Acetonitrile

**Diluent:** Acetonitrile and *Solution A* (5:95)

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

**Table 2**

| Time (min) | Solution A (%) | Solution B (%) |
|---|---|---|
| 0 | 100 | 0 |
| 7 | 95 | 5 |
| 20 | 90 | 10 |
| 30 | 75 | 25 |
| 35 | 50 | 50 |
| 40 | 50 | 50 |
| 41 | 100 | 0 |
| 50 | 100 | 0 |

**System suitability solution:** 0.2 mg/mL of USP Levetiracetam RS and 0.1 mg/mL of USP Levetiracetam Related Compound A RS in *Diluent* prepared as follows. Dissolve the required amount of USP Levetiracetam RS in 10% of the final volume of 0.1 N potassium hydroxide. Let the mixture react at room temperature for about 15 min, and then neutralize by adding 0.1 N hydrochloric acid at 10% of the flask volume. Add the required amount of USP Levetiracetam Related Compound A RS, sonicate to dissolve, and dilute with *Diluent* to volume. [Note—This solution contains levetiracetam, levetiracetam acid, and levetiracetam related compound A.]

**Standard solution:** 3 µg/mL of USP Levetiracetam RS in *Solution A*

**Sample solution:** Nominally 2 mg/mL of levetiracetam prepared as follows. Transfer a suitable volume of the Oral Solution to a suitable volumetric flask. Add 60% of the flask volume of *Solution A*, and sonicate at room temperature for 5 min with intermittent shaking. Allow the solution to cool, and dilute with *Solution A* to volume. Pass a portion of the solution through a suitable filter.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 210 nm

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

**Column temperature:** 45°

**Flow rate:** 1 mL/min

**Injection volume:** 20 µL

**System suitability**

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

**Suitability requirements**

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

**Tailing factor:** NMT 2.0, *Standard solution*

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

**Analysis**

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

Calculate the percentage of each impurity in the portion of Oral Solution taken:

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

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

$r_S$ = peak response of levetiracetam from the *Standard solution*

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

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

$F$ = relative response factor for each impurity (see *Table 3*)

**Acceptance criteria:** See *Table 3*.

**Table 3**

| Name | Relative Retention Time | Relative Response Factor | Acceptance Criteria, NMT (%) |
|---|---|---|---|
| Levetiracetam | 1.00 | — | — |
| Levetiracetam related compound A[a,b] | 1.38 | — | — |
| Levetiracetam acid[c] | 1.46 | 0.92 | 0.3 |
| Any individual unspecified degradation product | — | 1.0 | 0.10 |
| Total impurities | — | — | 1.0 |

[a] (*S*)-*N*-(1-Amino-1-oxobutan-2-yl)-4-chlorobutanamide.

[b] This is a process impurity and included for peak identification purposes only.

[c] (*S*)-2-(2-Oxopyrrolidin-1-yl)butanoic acid.

## SPECIFIC TESTS

***Change to read:***

• **pH** ⟨791⟩**:** 4.8–▲7.0▲ (RB 1-Dec-2019)

• **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 requirement of the test for absence of *Escherichia coli*.

## ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in light-resistant containers. Store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Levetiracetam RS

USP Levetiracetam Related Compound A RS

(*S*)-*N*-(1-Amino-1-oxobutan-2-yl)-4-chlorobutanamide.

$C_8H_{15}ClN_2O_2$ 206.67

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

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| LEVETIRACETAM ORAL SOLUTION | Documentary Standards Support | SM42020 Small Molecules 4 |

**Chromatographic Database Information:** Chromatographic Database

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