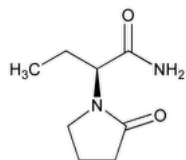


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Levetiracetam



$C_8H_{14}N_2O_2$ 170.21
1-Pyrrolidineacetamide, α -ethyl-2-oxo-, (α S)-;
(-)-(S)- α -Ethyl-2-oxo-1-pyrrolidineacetamide CAS RN®: 102767-28-2; UNII: 44YRR34555.

DEFINITION
Levetiracetam contains NLT 98.0% and NMT 102.0% of levetiracetam ($C_8H_{14}N_2O_2$), calculated on the anhydrous and solvent-free basis.

IDENTIFICATION
Change to read:

- A.** [▲ SPECTROSCOPIC IDENTIFICATION TESTS \(197\), Infrared Spectroscopy: 197K ▲](#) (CN 1-MAY-2020)
- B.** The retention time of the major peak of the *Identification solution* corresponds to that of the levetiracetam S-enantiomer from the *System suitability solution*, as obtained in the test for *Limit of Levetiracetam R-Enantiomer*.

ASSAY

- PROCEDURE**
Buffer: 2.7 g/L of monobasic potassium phosphate in water. Adjust with 2% aqueous potassium hydroxide (w/v) to a pH of 5.5.
Solution A: Acetonitrile and *Buffer* (1:19)
Solution B: Acetonitrile
Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
3	100	0
20	71	29

System suitability solution: 0.2 mg/mL of [USP Levetiracetam RS](#) and 0.08 mg/mL of [USP Levetiracetam Related Compound A RS](#) in *Solution A*. Prepare by first dissolving the required amount of [USP Levetiracetam RS](#) in a suitable volumetric flask. Add 10% of the flask 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, dilute with *Solution A* to volume, and mix. [NOTE—Levetiracetam related compound A is included for peak identification purposes.]

Standard solution: 0.1 mg/mL of [USP Levetiracetam RS](#) in *Solution A*

Sample solution: 0.1 mg/mL of Levetiracetam in *Solution A*

Chromatographic system
(See [Chromatography \(621\), System Suitability](#).)

Mode: LC
Detector: UV 205 nm
Column: 4.6-mm × 15-cm; packing L1
Flow rate: 0.9 mL/min
Injection volume: 10 µL

System suitability

Sample: *System suitability solution*

[NOTE—See [Table 2](#) for relative retention times.]

Suitability requirements

Relative standard deviation: NMT 1.0%, for the levetiracetam peak

[NOTE—If system suitability criteria cannot be met, it is recommended that the column temperature be maintained at 20° to stabilize the system.]

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of levetiracetam ($C_8H_{14}N_2O_2$) in the portion of Levetiracetam taken:

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

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

F = percentage of levetiracetam *R*-enantiomer from the test for *Limit of Levetiracetam R-Enantiomer*

Acceptance criteria: 98.0%–102.0% on the anhydrous and solvent-free basis

IMPURITIES

• [RESIDUE ON IGNITION \(281\)](#): NMT 0.1%

• **LIMIT OF LEVETIRACETAM *R*-ENANTIOMER**

Mobile phase: *n*-Hexane and dehydrated alcohol (80:20)

System suitability solution: 0.1 mg/mL of [USP Levetiracetam Racemic Mixture RS](#) in *Mobile phase*

Standard solution: 0.05 mg/mL of [USP Levetiracetam RS](#) in *Mobile phase*

Sample solution: 10 mg/mL of Levetiracetam in *Mobile phase*

Identification solution: 0.05 mg/mL of Levetiracetam from *Sample solution* 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: 1.0 mL/min

Injection volume: 20 μL

System suitability

Samples: *System suitability solution* and *Identification solution*

[NOTE—The relative retention times for levetiracetam *R*-enantiomer and levetiracetam *S*-enantiomer are 0.55 and 1.0, respectively. Use the chromatogram from the *Identification solution* for *Identification test B*.]

Suitability requirements

Resolution: NLT 4.0 between the *R*- and *S*-enantiomers, *System suitability solution*. [NOTE—If a loss of resolution (less than 4.0) is observed, it is recommended that the column temperature be maintained at 25° to stabilize the system.]

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of levetiracetam *R*-enantiomer in the portion of Levetiracetam taken:

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

r_U = peak response of levetiracetam *R*-enantiomer 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 = concentration of Levetiracetam in the *Sample solution* (mg/mL)

Acceptance criteria: NMT 0.8%

• **LIMIT OF LEVETIRACETAM RELATED COMPOUND B**

[NOTE—Perform this test only if levetiracetam related compound B is a known process impurity.]

Buffer: 1.22 g of sodium 1-decanesulfonate in 1 L of water containing about 1.3 mL of phosphoric acid. Adjust with 20% (w/v) potassium hydroxide to a pH of 3.0.