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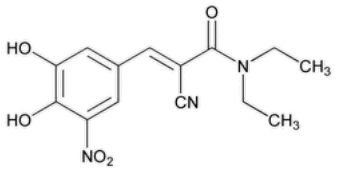
Entacapone



$C_{14}H_{15}N_3O_5$ 305.29

(*E*)-α-Cyano-*N*,*N*-diethyl-3,4-dihydroxy-5-nitrocinnamamide;

2-Propenamide, 2-cyano-3-(3,4-dihydroxy-5-nitrophenyl)-*N*,*N*-diethyl-,(*E*)- CAS RN®: 130929-57-6; UNII: 4975G9NM6T.

DEFINITION

Entacapone contains NLT 98.0% and NMT 102.0% of $C_{14}H_{15}N_3O_5$, calculated on the dried 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 *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Buffer: 2.34 g/L of monobasic sodium phosphate dihydrate. Adjust with phosphoric acid to a pH of 2.1.

Diluent: Methanol and tetrahydrofuran (7:3)

Mobile phase: Methanol, tetrahydrofuran, and *Buffer* (22:1:27)

System suitability solution: 1 µg/mL each of USP Entacapone Related Compound A RS and USP Entacapone RS in *Diluent*

Standard solution: 0.1 mg/mL of USP Entacapone RS in *Diluent*

Sample solution: 0.1 mg/mL of Entacapone in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 300 nm

Column: 4.6-mm × 25-cm; 5-µm packing L11

Flow rate: 1 mL/min

Injection size: 10 µL

System suitability

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

[Note—The relative retention times for entacapone related compound A and entacapone are 0.8 and 1.0, respectively.]

Suitability requirements

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

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{14}H_{15}N_3O_5$ in the portion of Entacapone 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 Entacapone RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

Inorganic Impurities

- **Residue on Ignition ⟨281⟩:** NMT 0.1%

Organic Impurities

- **Procedure**

Buffer, Diluent, and **Mobile phase:** Proceed as directed in the *Assay*.

Standard solution: Use the *System suitability solution* prepared as directed in the *Assay*.

Sample solution: 1.0 mg/mL of Entacapone in *Diluent*

Chromatographic system: Prepare as directed in the *Assay*.

Run time: 2 times the retention time of the entacapone peak

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between entacapone related compound A and entacapone

Relative standard deviation: NMT 10.0% based on the entacapone peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any individual impurity in the portion of Entacapone taken:

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

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

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

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

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

Acceptance criteria

Individual impurities: See *Impurity Table 1*.

Total impurities: NMT 0.2%

[Note—Do not include entacapone related compound A in the calculation of total impurities.]

Impurity Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Entacapone related compound A[a]	0.8	0.1
Entacapone	1.0	—
Any other unknown individual impurity	—	0.10
Total impurities	—	0.2

[a] (Z)-2-Cyano-3-(3,4-dihydroxy-5-nitrophenyl)-*N*,*N*-diethylacrylamide.

SPECIFIC TESTS

- **Loss on Drying ⟨731⟩**

Analysis: Dry 1.0 g of the sample in vacuum at a pressure not exceeding 49 mm of mercury at 65° to constant weight.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers, and store at room temperature.
- **USP Reference Standards ⟨11⟩**

USP Entacapone RS

USP Entacapone Related Compound A RS

(*Z*)-2-Cyano-3-(3,4-dihydroxy-5-nitrophenyl)-*N*,*N*-diethylacrylamide.

$C_{14}H_{15}N_3O_5$ 305.29

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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