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Entacapone Tablets

DEFINITION

Entacapone Tablets contain an amount of entacapone equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of entacapone ($C_{14}H_{15}N_3O_5$).

IDENTIFICATION

Change to read:

• **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020) **:** The sample shows a medium band at about 2216 cm^{-1} and strong bands at about 1628, 1604, 1544, 1512, 1440, 1376, 1348, 1296, 1280, and 1208 cm^{-1} similar to the reference preparation.

• **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**

Protect solutions from light.

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

Diluent: Methanol and tetrahydrofuran (70:30)

Mobile phase: Methanol, tetrahydrofuran, and *Buffer* (44:2:54)

Standard solution: 0.5 mg/mL of USP Entacapone RS in *Diluent*

Sample solution: Nominally 0.5 mg/mL of entacapone prepared as follows. Finely powder NLT 20 Tablets, and transfer a suitable portion of the powder to an appropriate volumetric flask. Add NLT 30% of the final flask volume of tetrahydrofuran, and sonicate for 3 min. Add NLT 30% of the final flask volume of methanol, and shake for 5 min. Dilute with methanol to volume. Centrifuge a portion of this solution, and use the supernatant.

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

Run time: 1.5 times the retention time of the entacapone peak

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 1.5%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of entacapone ($C_{14}H_{15}N_3O_5$) in the portion of Tablets 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 = nominal concentration of entacapone in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• Dissolution ⟨711⟩

Test 1

Medium: pH 5.5 phosphate buffer (6.8 g/L of monobasic potassium phosphate in water, adjusted with 1 M sodium hydroxide to a pH of 5.5); 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Standard stock solution: 0.22 mg/mL of USP Entacapone RS, prepared as follows. Transfer a suitable quantity of USP Entacapone RS to an appropriate volumetric flask, and dissolve in 2% of the flask volume of tetrahydrofuran. Dilute with *Medium* to volume. Protect this solution from light.

Standard solution: 0.022 mg/mL of USP Entacapone RS from the *Standard stock solution* in *Medium*. Protect this solution from light.

Sample solution: Pass a portion of the solution through a suitable filter of 20-µm pore size. Dilute with *Medium*, if necessary. Protect this solution from light.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV

Analytical wavelength: 313 nm

Path length: 1 cm

Blank: Tetrahydrofuran and *Medium* (0.2:99.8)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of entacapone ($C_{14}H_{15}N_3O_5$) dissolved:

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times V \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

L = label claim (mg/Tablet)

V = volume of *Medium*, 900 mL

Tolerances: NLT 80% (Q) of the labeled amount of entacapone ($C_{14}H_{15}N_3O_5$) is dissolved.

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium: pH 5.5 phosphate buffer (6.8 g/L of monobasic potassium phosphate in water, adjusted with 5 M sodium hydroxide to a pH of 5.5); 900 mL

Apparatus 2: 50 rpm

Time: 45 min

Standard stock solution: 0.45 mg/mL of USP Entacapone RS prepared as follows. Transfer a suitable quantity of USP Entacapone RS to an appropriate volumetric flask, and dissolve in 5% of the flask volume of methanol. Dilute with *Medium* to volume. Use this solution within 6.5 h.

Standard solution: 0.018 mg/mL of USP Entacapone RS from the *Standard stock solution* in *Medium*. Use this solution within 6.5 h.

Sample solution: Pass a portion of the solution under test through a suitable filter. Transfer 2 mL of the filtrate to a 25-mL volumetric flask, and dilute with *Medium* to volume. Pass the resulting solution through a suitable filter of 0.45-µm pore size. Use this solution within 6.5 h.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV

Analytical wavelength: 313 nm

Path length: 1 cm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of entacapone ($C_{14}H_{15}N_3O_5$) dissolved:

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times V \times D \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

L = label claim (mg/Tablet)

V = volume of *Medium*, 900 mL

D = dilution factor for the *Sample solution,* 12.5

Tolerances: NLT 80% (Q) of the labeled amount of entacapone ($C_{14}H_{15}N_3O_5$) is dissolved.

Test 3: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

Medium: pH 5.5 phosphate buffer (6.8 g/L of monobasic potassium phosphate and 0.05 g/L of sodium hydroxide in water, adjusted with 5 M sodium hydroxide to a pH of 5.5); 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Standard stock solution: 0.45 mg/mL of USP Entacapone RS prepared as follows. Transfer a suitable quantity of USP Entacapone RS to an appropriate volumetric flask, and dissolve in 30% of the flask volume of methanol. Sonicate to dissolve, and allow the solution to cool to room temperature. Dilute with methanol to volume. Use this solution within 6 h.

Standard solution: 0.009 mg/mL of USP Entacapone RS from the *Standard stock solution* in *Medium*. Use this solution within 6 h.

Sample stock solution: Pass a portion of the solution through a suitable filter of 0.45-µm pore size. Use this solution within 6 h.

Sample solution: Transfer 2.0 mL of the *Sample stock solution* to a 50-mL volumetric flask, and dilute with *Medium* to volume. Use this solution within 6 h.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV

Analytical wavelength: 378 nm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of entacapone ($C_{14}H_{15}N_3O_5$) dissolved:

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times V \times D \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

L = label claim (mg/Tablet)

V = volume of *Medium*, 900 mL

D = dilution factor for the *Sample solution,* 25

Tolerances: NLT 70% (Q) of the labeled amount of entacapone ($C_{14}H_{15}N_3O_5$) is dissolved.

• **Uniformity of Dosage Units** ⟨905⟩**:** Meet the requirements

IMPURITIES

• **Organic Impurities**

Protect solutions from light.

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

System suitability solution: 0.03 mg/mL each of USP Entacapone RS and USP Entacapone Related Compound A RS in *Diluent*

Standard solution: 0.003 mg/mL of USP Entacapone RS in *Diluent*

Sample solution: Nominally 3 mg/mL of entacapone prepared as follows. Finely powder NLT 20 Tablets, and transfer a suitable portion of the powder to an appropriate volumetric flask. Add NLT 30% of the final flask volume of tetrahydrofuran, and sonicate for 3 min. Add NLT 30% of the final flask volume of methanol, and shake for 5 min. Dilute with methanol to volume. Centrifuge a portion of this solution, and use the supernatant within 7 h.

System suitability

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

Suitability requirements

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

Relative standard deviation: NMT 10.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

r_U = peak response of each 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 = nominal concentration of entacapone in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Entacapone related compound A	0.8	0.2
Entacapone	1.0	—
Any individual unspecified degradation product	—	0.1
Total impurities[a]	—	0.2

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

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in light-resistant containers. Store at controlled room temperature.
- **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
- **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 TABLETS	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

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