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Tolcapone Tablets

DEFINITION

Tolcapone Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of tolcapone ($C_{14}H_{11}NO_5$).

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197D**▲ (CN 1-May-2020)

Wavelength range: Between 2200 and 1090 cm^{-1}

Sample: Grind 10 Tablets to a fine powder.

Analysis: Transfer an amount of powder equivalent to 3 mg of tolcapone into a polystyrene vial containing 2 mixing beads. Add 300 mg of IR-grade potassium bromide, and disperse the material in the matrix by agitating the capped vial in a grinding mill for 2 min. Transfer a portion of the material to a sample cup. Record the diffuse reflectance IR spectrum.

Acceptance criteria: The spectrum thus obtained exhibits maxima only at the same wavelengths as those of a similar preparation of USP Tolcapone RS, concomitantly measured.

• **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**

Diluent 1: Methanol and acetonitrile (24:15)

Diluent 2: Acetonitrile, methanol, and water (25:40:35)

Buffer: Transfer 6.8 g of monobasic potassium phosphate into a 1-L volumetric flask. Dissolve in about 980 mL of water. Adjust with phosphoric acid to a pH of 2.0. Dilute with water to volume.

Mobile phase: Acetonitrile, methanol, and *Buffer* (25:40:35)

System suitability solution: 100 µg/mL of USP Tolcapone RS, 10 µg/mL of USP Tolcapone Related Compound A RS, and 10 µg/mL of USP Tolcapone Related Compound B RS in *Diluent 2*

Standard stock solution: 1.0 mg/mL of USP Tolcapone RS in *Diluent 1*

Standard solution: 0.1 mg/mL of USP Tolcapone RS from *Standard stock solution* prepared as follows. Transfer a suitable volume of *Standard stock solution* to a suitable volumetric flask. Add 55% of the flask volume of *Diluent 1* and dilute with water to volume.

Sample stock solution: Nominally 1.0 mg/mL of tolcapone from NLT 20 Tablets prepared as follows. Finely powder the Tablets and transfer a portion of the powder equivalent to NLT 100 mg of tolcapone to a suitable volumetric flask, add 10% of the flask volume of water, and sonicate for 10 min. Add 65% of the flask volume of *Diluent 1*, and sonicate for 15 min. Allow the sample to settle. If the material is still undispersed, sonicate for an additional 5 min. Dilute with water to volume, and mix. Centrifuge a portion of this solution.

Sample solution: Nominally 0.1 mg/mL of tolcapone from the centrifuged *Sample stock solution* prepared as follows. Transfer a suitable volume of the *Sample stock solution* to a suitable volumetric flask. Dilute with *Diluent 2* to volume. Pass a portion of the solution through a filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 4.0-mm × 25-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

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

[Note—The relative retention times are given in *Table 1*.]

Suitability requirements

Resolution: NLT 4.0 between tolcapone related compound B and tolcapone, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of tolcapone ($C_{14}H_{11}NO_5$) 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 Tolcapone RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: pH 6.8 phosphate buffer containing 1% of sodium lauryl sulfate; 900 mL

Apparatus 2: 75 rpm

Time: 30 min

Standard stock solution: 1 mg/mL of USP Tolcapone RS prepared as follows. Transfer a suitable quantity of USP Tolcapone RS to a suitable volumetric flask. Add 10% of the flask volume of methanol. Dissolve and dilute with *Medium* to volume.

Standard solution: (*L*/1000) mg/mL of USP Tolcapone RS from a suitable volume of *Standard stock solution* in *Medium*, where *L* is the label claim, in mg/Tablet

Sample solution: Filter portions of the solution under test, suitably diluted with *Medium* if necessary.

Instrumental conditions

Mode: UV

Analytical wavelength: 271 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of tolcapone ($C_{14}H_{11}NO_5$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times D \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = volume of *Medium*, 900 mL

D = dilution factor if dilution was necessary

L = label claim (mg/Tablet)

Tolerances: NLT 75% (*Q*) of the labeled amount of tolcapone ($C_{14}H_{11}NO_5$) is dissolved.

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

IMPURITIES

• **Organic Impurities**

Diluent 1, Diluent 2, Mobile phase, System suitability solution, Standard solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each degradation product in the portion of Tablets taken:

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

r_U = peak area of any degradation product in the *Sample solution*

r_S = peak area of tolcapone in the *Standard solution*

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

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

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Tolcapone related compound A[a]	0.6	—
Tolcapone	1.0	—
Tolcapone related compound B[a]	1.4	—
Any individual unspecified degradation product	—	0.1
Total degradation products	—	0.5

[a] Process impurity, controlled in the drug substance, and included for information only. Not to be included in total degradation products.

ADDITIONAL REQUIREMENTS

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

USP Tolcapone RS

USP Tolcapone Related Compound A RS
4'-Methyl-3,4-dihydroxybenzophenone.
$C_{14}H_{12}O_3$ 228.24

USP Tolcapone Related Compound B RS
4-Hydroxy-3-methoxy-4'-methyl-5-nitrobenzophenone.
$C_{15}H_{13}NO_5$ 287.27

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

Topic/Question	Contact	Expert Committee
TOLCAPONE TABLETS	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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