Entacapone Tablets

エンタカポン錠

Entacapone Tablets contain not less than 95.0% and not more than 105.0% of the labeled amount of entacapone ($C_{14}H_{15}N_3O_5$: 305.29).

Method of preparation Prepare as directed under Tablets, with Entacapone.

Identification To 1 mL of the sample solution obtained in the Assay add methanol to make exactly 50 mL. Determine the absorption spectrum of this solution as directed under Ultraviolet-visible Spectrophotometry *<2.24>*: it exhibits a maximum at about 303 nm.

Uniformity of dosage unit *<6.02>* Perform the Mass variation test, or the Content uniformity test according to the following method: it meets the requirement.

Conduct this procedure using light-resistant vessels. To 1 tablet of Entacapone Tablets add 70 mL of methanol, shake for 5 minutes, and add 60 mL of tetrahydrofuran. Sonicate for 3 minutes, shake for 5 minutes, and add methanol to make exactly 200 mL. Centrifuge this solution, pipet *V* mL of the supernatant liquid, add methanol to make exactly *V'* mL so that each mL contains about 0.5 mg of entacapone ($C_{14}H_{15}N_3O_5$), and use this solution as the sample solution. Separately, weigh accurately about 50 mg of Entacapone RS (separately determine the loss on drying *<2.41>* under the same conditions as Entacapone), dissolve in 30 mL of tetrahydrofuran, add methanol to make exactly 100 mL, and use this solution as the standard solution. Perform the test with exactly 10 μL each of the sample solution and standard solution as directed under Liquid Chromatography *<2.01>* according to the following conditions, and determine the peak areas, A_T and A_S of entacapone in each solution.

$$\text{Amount (mg) of entacapone } (C_{14}H_{15}N_3O_5) = M_S \times A_T / A_S \times V'/V \times 2$$

M_S: Amount (mg) of Entacapone RS taken, calculated on the dried basis

Operating conditions —

Detector, column, column temperature, mobile phase and flow rate: Proceed as directed in the operating conditions in the Assay.

System suitability —

System performance and system repeatability: Proceed as directed in the system suitability in the Assay.

Dissolution *<6.10>* When the test is performed at 50 revolutions per minute according to the Paddle method, using 900 mL of 0.05 mol/L potassium dihydrogen phosphate TS, adjusted to pH 5.5 with sodium hydroxide TS, as the dissolution medium, the dissolution rate in 30 minutes of Entacapone Tablets is not less than 80%.

Start the test with 1 tablet of Entacapone Tablets, withdraw not less than 15 mL of the medium at the specified minute after starting the test, and filter through a membrane filter with a pore size not exceeding 0.45 μm. Discard the first 5 mL of the filtrate, pipet *V* mL of the subsequent filtrate, add the dissolution medium to make exactly *V'* mL so that each mL contains about 11 μg of entacapone ($C_{14}H_{15}N_3O_5$), and use this solution as the sample solution. Separately, weigh accurately about 22 mg of Entacapone RS (separately determine the loss on drying *<2.41>* under the same conditions as Entacapone), add 4 mL of methanol, dissolve by sonicating, and add the dissolution medium to make exactly 200 mL. Pipet 5 mL of this solution, add the dissolution medium to make exactly 50 mL, and use this solution as the standard solution. Determine the absorbances, A_T and A_S, of the sample solution and standard solution at 313 nm as directed under Ultraviolet-visible Spectrophotometry *<2.24>*, using the dissolution medium as the blank.

$$\text{Dissolution rate (\%) with respect to the labeled amount of entacapone } (C_{14}H_{15}N_3O_5) = M_S \times A_T / A_S \times V'/V \times 1/C \times 45$$

M_S: Amount (mg) of Entacapone RS taken, calculated on the dried basis

C: Labeled amount (mg) of entacapone ($C_{14}H_{15}N_3O_5$) in 1 tablet

Assay Conduct this procedure using light-resistant vessels. Weigh accurately the mass of not less than 20 Entacapone Tablets, and powder. Weigh accurately a portion of the powder, equivalent to about 0.1 g of entacapone ($C_{14}H_{15}N_3O_5$), add 60 mL of tetrahydrofuran, and sonicate for 3 minutes. Add 60 mL of methanol, shake for 5 minutes, and add methanol to make exactly 200 mL. Centrifuge this solution, and use the supernatant liquid as the sample solution. Separately, weigh accurately about 50 mg of Entacapone RS (separately determine the loss on drying *<2.41>* under the same conditions as Entacapone), dissolve in 30 mL of tetrahydrofuran, add methanol to make exactly 100 mL, and use this solution as the standard solution. Perform the test with exactly 10 μL each of the sample solution and standard solution as directed under Liquid Chromatography *<2.01>* according to the following conditions, and determine the peak areas, A_T and A_S of entacapone in each solution.

$$\text{Amount (mg) of entacapone } (C_{14}H_{15}N_3O_5) = M_S \times A_T / A_S \times 2$$

M_S: Amount (mg) of Entacapone RS taken, calculated on the dried basis

Operating conditions —

Detector: An ultraviolet absorption photometer (wavelength: 300 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 25 cm in length, packed with phenylated silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 25℃.

Mobile phase: Dissolve 2.34 g of sodium dihydrogenphosphate dihydrate in water, add exactly 2 mL of phosphoric acid, and add water to make 1000 mL. To 540 mL of this solution add 440 mL of methanol and 20 mL of tetrahydrofuran.

Flow rate: Adjust so that the retention time of entacapone is about 12 minutes.

System suitability—

System performance: To 20 mL of the standard solution add a mixture of methanol and tetrahydrofuran (7:3) to make 50 mL, and use this solution as the solution for system suitability test. Separately, dissolve 20 mg of Entacapone Related Substance A RS for System Suitability in 30 mL of tetrahydrofuran, and add methanol to make 100 mL. To 15 mL of this solution and 15 mL of the solution for system suitability test add a mixture of methanol and tetrahydrofuran (7:3) to make 100 mL. When the procedure is run with 10 μL of this solution under the above operating conditions, the related substance A, having the relative retention time of about 0.8 to entacapone, and entacapone are eluted in this order with the resolution between these peaks being not less than 2.0.

System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of entacapone is not more than 1.0%.

Containers and storage Containers– Tight containers.

Others

Related substance A: refer to it described in Entacapone.

Add the following to 9.01 Reference Standards (1):

Entacapone RS

Entacapone Related Substance A RS for System Suitability