Zolpidem Tartrate Tablets

Dissolution <*6.10*> Perform the test with 1 tablet of Zolpidem Tartrate Tablets at 50 revolutions per minute according to the Paddle method, using 900 mL of water as the dissolution medium. Withdraw not less than 20 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 10 mL of the filtrate, pipet V mL of the subsequent filtrate, add 2nd fluid for dissolution test to make exactly V' mL so that each mL contains about 2.8 μg of zolpidem tartrate ($C_{19}H_{21}N_3O.1/2\ C_4H_6O_6$) according to the labeled amount, and use this solution as the sample solution. Separately, weigh accurately about 22 mg of Zolpidem Tartrate RS (previously determine the water <*2.48*> with 0.5 g by direct titration in volumetric titration), and dissolve in water to make exactly 100 mL. To exactly 5 mL of this solution add water to make exactly 200 mL. Pipet 25 mL of this solution, add 2nd fluid for dissolution test 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 242 nm as directed under Ultraviolet-visible Spectrophotometry <*2.24*>, using diluted 2nd fluid for dissolution test as the blank.

The requirements are met if Zolpidem Tartrate Tablets conform to the dissolution requirements.

Dissolution rate (%) with respect to the labeled amount of zolpidem tartrate ($C_{19}H_{21}N_3O.1/2\ C_4H_6O_6$)

$= M_S \times A_T/A_S \times V'/V \times 1/C \times 45/4$

M_S: Amount (mg) of Zolpidem Tartrate RS, calculated on the anhydrous basis

C: Labeled amount (mg) of zolpidem tartrate ($C_{19}H_{21}N_3O.1/2\ C_4H_6O_6$) in 1 tablet

Dissolution Requirements

Labeled amount	Specified minute	Dissolution rate
5 mg	15 minutes	Not less than 80%
10 mg	15 minutes	Not less than 80%

Zolpidem Tartrate RS $C_{19}H_{21}N_3O.1/2\ C_4H_6O_6$: 382.44

(+)-*N,N*,6-trimethyl-2-*p*-tolylimidazo[1,2-a]pyridine-3-acetamide 1/2 L-tartrate. It meets the following requirement. Purify by the following method if needed.

Purification method—Dissolve 60 g of zolpidem tartrate in water, and make alkaline with sodium hydroxide TS. Collect the produced precipitate, and wash with water. Recrystallize from 2-propanol, dry in vacuum at 60ºC, and obtain about 35 g of zolpidem base. Dissolve 12.0 g of the zolpidem base

so obtained in methanol and add a solution prepared by dissolving 2.94 g of tartaric acid in methanol. After cooling, collect the produced precipitate, wash with methanol, dry in vacuum at 75ºC, and obtain about 12 g of Zolpidem Tartrate RS.

Description —Zolpidem Tartrate RS occurs as a while crystalline powder.

Optical rotation <*2.49*> $[\alpha]_D^{20}$: about +1.8° (1 g, *N*,*N*-dimethylformamide, 20 mL, 100 mm).

Identification:

(1) Determine the infrared absorption spectrum of Zolpidem Tartrate RS as directed in the diffuse reflectance method under Infrared Spectrophotometry <*2.25*>: it exhibits absorption at the wave numbers of about 3540 cm^{-1}, 3460 cm^{-1}, 1635 cm^{-1}, 1123 cm^{-1}, 853 cm^{-1}, 835 cm^{-1} and 797 cm^{-1}. To 1 to 2 mg of Zolpidem Tartrate RS add 0.3 to 0.4 g of potassium bromide for infrared absorption spectrum.

(2) Determine the spectrum of Zolpidem Tartrate RS in deuterated dimethylsulfoxide for nuclear magnetic resonance spectroscopy (1 in 25) as directed under Nuclear Magnetic Resonance Spectroscopy <*2.21*> (^{13}C), using tetramethylsilane for nuclear magnetic resonance spectroscopy as a reference compound: it exhibits a signal at around δ28.8 ppm, δ35.2 ppm, δ36.9 ppm, δ72.0 ppm and δ120.7ppm.

Related substances —Dissolve 10 mg of Zolpidem Tartrate RS in 20 mL of methanol, and use this solution as the sample solution. To exactly 1 mL of this solution add methanol to make exactly 100 mL. Pipet 2 mL of this solution, add methanol to make exactly 20 mL, and use this solution as the standard solution. Perform the test with 5 μL each of the sample solution and standard solution as directed under Liquid Chromatography <*2.01*> according to the following conditions. Determine each peak area by the automatic integration method: the total area of the peaks other than zolpidem from the sample solution is not larger than the peak area of zolpidem from the standard solution.

Operating conditions

Detector: An ultraviolet absorption photometer (wavelength: 254 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 7.5 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 25ºC.

Mobile phase: To 4.9 g of phosphoric acid add 1000 mL of water, and adjust to pH 5.5 with triethylamine. To 550 mL of this solution add 250 mL of methanol and 200 mL of acetonitrile.

Flow rate: Adjust the flow rate so that the retention time of zolpidem is about 5 minutes.

Time span of measurement: About 5 times as long as the retention time of zolpidem beginning after the solvent peak.

System suitability

Test for required detectability: Dissolve 10 mg of Zolpidem Tartrate RS in 20 mL of methanol. Pipet 1 mL of this solution, add methanol to make exactly 100 mL, and use this solution as the solution for system suitability test. To exactly 2 mL of this solution add methanol to make exactly 20 mL. Confirm

that the peak area of zolpidem obtained from 5 μL of this solution is equivalent to 7 to 13% of that from 5 μL of the solution for system suitability test.

System performance: When the procedure is run with 5 μL of a solution, prepared by dissolving 10 mg each of zolpidem tartrate and benzyl parahydroxybenzoate in 100 mL of methanol, under the above operating conditions, zolpidem and benzyl parahydroxybenzoate are eluted in this order with the resolution between these peaks being not less than 9.

System repeatability: When the test is repeated 6 times with 5 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of zolpidem is not more than 5.0%.

Water <*2.48*>: not more than 3.0%. (0.5g, volumetric titration, direct titration).

Content: not less than 99.0%, calculated on the dehydrated basis. Assay－Weigh accurately about 0.4 g of Zolpidem Tartrate RS, dissolve in 100 mL of a mixture of acetic anhydride and acetic acid (100), and titrate <*2.50*> with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination in the same manner, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 38.24 mg of $C_{19}H_{21}N_3O.1/2\ C_4H_6O_6$