Granisetron Hydrochloride Tablets

Dissolution <*6.10*> Perform the test with 1 tablet of Graniserton Hydrochloride Tablets at 50 revolutions per minute according to the Paddle method, using 900 mL of 2nd fluid for dissolution test as the dissolution medium. Start the test, 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 1.1 μg of granisetron ($C_{18}H_{24}N_4O$) according to the labeled amount, and use this solution as the sample solution. Separately, weigh accurately about 25 mg of Granisetron Hydrochloride RS (separately, determine the water <*2.48*> with 1 g by direct titration in volumetric titration), and dissolve in 2nd fluid for dissolution test to make exactly 200 mL. Pipet 2 mL of this solution, add 2nd fluid for dissolution test to make exactly 200 mL, and use this solution as the standard solution. Perform the test with exactly 50 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 granisetron of both solutions.

The requirements are met if Granisetron Hydrochloride Tablets conform to the dissolution requirements.

Dissolution rate (%) with respect to the labeled amount of granisetron ($C_{18}H_{24}N_4O$)

$= M_S \times A_T/A_S \times V'/V \times 1/C \times 9/2 \times 0.895$

M_S: Amount (mg) of Granisetron Hydrochloride RS, calculated on the anhydrous basis

C: Labeled amount (mg) of granisetron ($C_{18}H_{24}N_4O$) in 1 tablet

Operating conditions—

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

Column: A stainless steel column 4.6 mm in inside diameter and 15 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: Dissolve 15.6 g of sodium dihydrogen phosphate dehydrate in 900 mL of water, adjust the pH to 2.0 with phosphoric acid, and add water to make 1000 mL. To 750 mL of this solution add 240 mL of methanol, and add 11 mL of tetrahydrofuran.

Flow rate: Adjust the flow rate so that the retention time of granisetron is about 10 minutes.

System suitability—

System performance: When the procedure is run with 50 μL of the standard solution under the

above operating conditions, the number of theoretical plates and the symmetry factor of the peak of granisetron are not less than 3000 and not more than 2.0, respectively.

System repeatability: When the test is repeated 6 times with 50 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of granisetron is not more than 1.5%.

Dissolution Requirements

Labeled amount*	Specified minute	Dissolution rate
1 mg	15 minutes	Not less than 85%
2 mg	15 minutes	Not less than 85%

*as Granisetron

Granisetron Hydrochloride RS $C_{18}H_{24}N_4O \cdot HCl$: 348.87 1-methyl-*N*-(endo-9-methyl-9-azabicyclo-[3.3.1]non-3-yl)-1*H*-indazole-3-carboxamide hydrochloride. It meets the following requirements. Purify according to the following method if needed.

Purification method−To 225 g of Granisetron Hydrochloride add 3200 mL of 2-propanol, boil under a reflux condenser, cool with 31 mL of water to about 20ºC, and obtain the precipitate. Remove the water by distilling with 2-propanol under reduced pressure, filter, wash the precipitate so obtained with 2-propanol, and dry at about 40ºC.

Description−Granisetron Hydrochloride RS occurs as a white, crystalline powder.

Identification−Determine the infrared absorption spectrum of Granisetron Hydrochloride RS as directed in the paste method under Infrared Spectrophotometry <2.25>: it exhibits absorption at the wave numbers of about 3230 cm^{-1}, 2630 cm^{-1}, 1645 cm^{-1}, 1546 cm^{-1}, 1309 cm^{-1} and 756 cm^{-1}.

Water <2.48>: not more than 0.5% (1 g, volumetric titration, direct titration).

Content: not less than 99.0%. Assay−Weigh accurately about 50 mg of Granisetron Hydrochloride RS, dissolve in 30 mL of a mixture of acetic anhydride and acetic acid (100) (7:3), 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
= 34.89 mg of $C_{18}H_{24}N_4O \cdot HCl$