

Granisetron Hydrochloride Fine Granules

Dissolution <6.10> Weigh accurately an amount of Granisetron Hydrochloride Fine Granules, equivalent to about 2 mg of granisetron ($C_{18}H_{24}N_4O$) according to the labeled amount, and perform the test at 50 revolutions per minute according to the Paddle method, using 900 mL of water 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 μ m. Discard the first 10 mL of the filtrate, and use the subsequent filtrate 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 the water to make exactly 200 mL. Pipet 2 mL of this solution, add water to make exactly 100 mL, and use this solution as the standard solution. Perform the test with exactly 50 μ L 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 Fine Granules conform to the dissolution requirements.

$$\begin{aligned} &\text{Dissolution rate (\%)} \text{ with respect to the labeled amount of granisetron } (C_{18}H_{24}N_4O) \\ &= M_S/M_T \times A_T/A_S \times 1/C \times 9 \times 0.895 \end{aligned}$$

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

M_T : Amount (g) of sample

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

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 μ m in particle diameter).

Column temperature: A constant temperature of about 25°C.

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 μ L 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
4 mg/g	15 minutes	Not less than 85%

*as Granisetron

Granisetron Hydrochloride RS $\text{C}_{18}\text{H}_{24}\text{N}_4\text{O}\cdot\text{HCl}$: 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 20°C, 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 40°C.

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 $\text{C}_{18}\text{H}_{24}\text{N}_4\text{O}\cdot\text{HCl}$