Pranlukast Capsules

Dissolution <*6.10*> Perform the test with 1 capsule of Pralunkast Capsules at 100 revolutions per minute according to the Paddle method, using 900 mL of a solution, prepared by adding 2nd fluid for dissolution test to 1 g of polysorbate 80 to make 200 mL, 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 a solution, prepared by adding 2nd fluid for dissolution test to 1 g of polysorbate 80 to make 200 mL, to make exactly *V′* mL, so that each mL contains about 0.5 μg of pranlukast hydrate ($C_{27}H_{23}N_5O_4 \cdot 1/2\ H_2O$) according to the labeled amount, and use this solution as the sample solution. Separately, weigh accurately about 25 mg of Pranlukast RS (separately, determine the loss on drying <*2.41*>, previously dried at 105ºC for 2 hours), dissolve in 5 mL of dimethylsulfoxide, and add a solution, prepared by adding 2nd fluid for dissolution test to 1 g of polysorbate 80 to make 200 mL, to make exactly 100 mL. Pipet 2 mL of this solution, add a solution, prepared by adding 2nd fluid for dissolution test to 1 g of polysorbate 80 to make 200mL, to make exactly 100 mL, and use this solution as the standard solution. Determine the absorbances, A_T and A_S, at 260 nm of the sample solution and standard solution as directed under Ultraviolet-visible Spectrophotometry <*2.24*>, using a solution by adding 2nd fluid for dissolution test to 1 g of polysorbate 80 to make 200 mL, as the blank.

The requirements are met if Pranlukast Capsules conform to the dissolution requirements.

Dissolution rate (%) with respect to the labeled amount of pranlukast hydrate

$= M_S \times A_T/A_S \times V'/V \times 1/C \times 18 \times 1.0187$

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

C: Labeled amount (mg) of pranlukast hydrate ($C_{27}H_{23}N_5O_4 \cdot 1/2\ H_2O$) in 1 capsule

Dissolution Requirements

Labeled amount	Specified minute	Dissolution rate
112.5 mg	90 minutes	Not less than 80%

Pranlukast RS $C_{27}H_{23}N_5O_4$: 481.50 4-oxo-8-[4-(4-phenylbutoxy)benzoylamino]-2-(tetrazol-5-yl)-4*H*-1-benzopyran. It meets the following requirements.

Purification method−Dissolve pranlukast hydrate in *N*,*N*-dimethylformamide, and add ethanol (99.5) to induce the crystallization. Repeat this procedure twice, dry the crystals so obtained at 60ºC for 24 hours under reduced pressure, and obtain Pranlukast RS.

Description−Pranlukast RS occurs as white to light yellow crystalline powder.

Identification (1) Determine the absorption spectrum of a solution of Pranlukast RS in ethanol (99.5) (1 in 100000) as directed under Ultraviolet-visible Spectrophotometry <*2.24*>: it exhibits a maximum between 256 nm and 260 nm, and a shoulder between 310 nm and 318 nm.

(2) Determine the infrared absorption spectrum of Pranlukast RS as directed in the potassium bromide disk method under Infrared Spectrophotometry <*2.25*>: it exhibits absorption at the wave numbers of about 3100 cm^{-1}, 2940 cm^{-1}, 1662 cm^{-1}, 1646 cm^{-1}, and 1254 cm^{-1}.

Absorbance <*2.24*> $E_{1cm}^{1\%}$ (258 nm): 855 − 875 (10 mg, calculated on the dried basis, ethanol (99.5), 1000 mL).

Related substances−Perform the test with 4 μL of a solution of Pranlukast RS in a mixture of acetonitrile and dimethylsulfoxide (3:1) (1 in 5000) as directed under Liquid Chromatography <*2.01*>, and determine the peak area by the automatic integration method: the total area of the peaks of related substances other than pranlukast is not more than 0.5%.

Operating conditions

Detector: An ultraviolet absorption photometer (wavelength: 260 nm).

Column: A stainless steel column about 6 mm in inside diameter and about 15 cm in length, packed with octylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 25ºC.

Mobile phase: A mixture of 0.02 mol/L potassium dihydrogen phosphate TS, acetonitrile and methanol (5:5:1).

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

Time span of measurement: About 2 times as long as the retention time of pranlukast beginning after the solvent peak.

Selection of column: When the procedure is run with 4 μL of a solution prepared by adding 1 mL of a solution of a mixture of acetonitrile and dimethylsulfoxide in isoamyl parahydroxybenzoate (3:1) (1 in 2500) to 1 mL of a solution of a mixture of acetonitrile and dimethylsulfoxide in Pranlukast RS (3:1) (1 in 2500) under the above operating conditions, use a column giving elution of pranlukast and isoamyl parahydroxybenzoate in this order with the resolution between these peaks being not less than 3.

Detection sensitivity: When the procedure is run with 4 μL of a solution of a mixture of acetonitrile and dimethylsulfoxide (3:1) in Pranlukast RS (1 in 1000000), adjust the detection sensitivity so that the peak height of pranlukast is 1 to 2% of the full-scale.

Loss on drying <*2.41*>: not more than 2.0% (0.5 g, 105ºC, 2 hours).

Content: not less than 99.0%, calculated on the anhydrous basis. Assay−Weigh accurately about 0.3 g of Pranlukast RS, dissolve in 30 mL of *N*,*N*-dimethylformamide, and titrate <*2.50*> with 0.1 mol/L tetramethylammonium hydroxide VS (indicator: 1 mL of thymol blue-*N*,*N*-dimethylformamide TS) until the color of the solution changes from yellow through yellow-green to blue-green. Perform a blank determination in the same manner, and make any necessary correction.

Each mL of 0.1 mol/L tetramethylammonium hydroxide VS
= 48.15 mg of $C_{27}H_{23}N_5O_4$