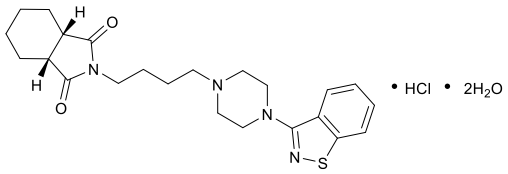
Perospirone Hydrochloride Hydrate

ペロスピロン塩酸塩水和物



$C_{23}H_{30}N_4O_2S.HCl.2H_2O$: 499.07

(3a*R*,7a*S*)-2-{4-[4-(1,2-Benzothiazol-3-yl)piperazin-1-yl]butyl}hexahydro-1*H*-isoindole-1,3(2*H*)-dione monohydrochloride dihydrate

[*192052-81-6*]

Perospirone Hydrochloride Hydrate contains not less than 98.0% and not more than 102.0% of perospirone hydrochloride ($C_{23}H_{30}N_4O_2S.HCl$: 463.04), calculated on the anhydrous basis.

Description Perospirone Hydrochloride Hydrate occurs as white, crystals or crystalline powder.

It is soluble in methanol, and slightly soluble in water and in ethanol (99.5).

Identification (1) Determine the absorption spectrum of a solution of Perospirone Hydrochloride Hydrate in methanol (3 in 125,000) as directed under Ultraviolet-visible Spectrophotometry *<2.24>*, and compare the spectrum with the Reference Spectrum or the spectrum of a solution of Perospirone Hydrochloride RS prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelengths.

(2) Determine the infrared absorption spectrum of Perospirone Hydrochloride Hydrate as directed in the potassium bromide disk method under Infrared Spectrophotometry *<2.25>*, and compare the spectrum with the Reference Spectrum or the spectrum of Perospirone Hydrochloride RS: both spectra exhibit similar intensities of absorption at the same wave numbers.

(3) A solution of Perospirone Hydrochloride Hydrate (1 in 2000) responds to Qualitative Tests *<1.09>* for chloride.

Purity Related substances—Dissolve about 60 mg of Perospirone Hydrochloride Hydrate in 50 mL of the mobile phase, and use this solution as the sample solution. Perform the test with 10 μL of the sample solution as directed under Liquid Chromatography *<2.01>* according to the following conditions. Determine each peak area by the automatic integration method, and calculate the amounts of them by the area percentage method: the amount of each related substance to perospirone is less than 0.10%. For the areas of the peaks, having the relative retention times of about 0.64 and about 1.57 to perospirone, multiply their correction factors, 1.3 and 3.1, respectively.

Operating conditions—

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

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

System suitability—

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

Test for required detectability: Pipet 1 mL of the sample solution, and add the mobile phase to make exactly 100 mL. Pipet 10 mL of this solution, and add the mobile phase to make exactly 100 mL. Confirm that the peak area of perospirone obtained with 10 μL of this solution is equivalent to 0.07 to 0.13% of that with 10 μL of the sample solution.

System repeatability: To 1 mL of the sample solution add the mobile phase to make 100 mL. To 10 mL of this solution add the mobile phase to make 100 mL. When the test is repeated 6 times with 10 μL of this solution under the above operating conditions, the relative standard deviation of the peak area of perospirone is not more than 1.0%.

Water *<2.48>* 6.8 – 7.6% (50 mg, coulometric titration).

Residue on ignition *<2.44>* Not more than 0.1% (1 g).

Assay Weigh accurately about 60 mg each of Perospirone Hydrochloride Hydrate and Perospirone Hydrochloride RS (separately determine the water *<2.48>* in the same manner as Perospirone Hydrochloride Hydrate), add exactly 10 mL each of the internal standard solution, add the mobile phase to make 50 mL, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with 10 μL each of the sample solution and standard solution as directed under Liquid Chromatography *<2.01>* according to the following conditions, and calculate the ratios, Q_T and Q_S, of the peak area of perospirone to that of the internal standard.

Amount (mg) of perospirone hydrochloride ($C_{23}H_{30}N_4O_2S.HCl$)

$= M_S \times Q_T / Q_S$

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

Internal standard solution—A solution of 4′-methoxyacetophenone in the mobile phase (1 in 275).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 220 nm).

Column: A stainless steel column 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 25°C.

Mobile phase: Dissolve 1.0 g of sodium 1-heptane sulfonate in 950 mL of water, adjust to pH 2.5 with phosphoric acid, and add water to make 1000 mL. To 750 mL of this solution add 400 mL of acetonitrile for liquid chromatography and 100 mL of methanol for liquid chromatography.

Flow rate: Adjust so that the retention time of perospirone is about 20 minutes.

System suitability—

System performance: When the procedure is run with 10 μL of the standard solution under the above operating conditions, the internal standard and perospirone are eluted in this order with the resolution between these peaks being not less than 4.

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 ratio of the peak area of perospirone to that of the internal standard is not more than 1.0%.

Containers and storage Containers—Tight containers.

Add the following to 9.01 Reference Standards (1):

Perospirone Hydrochloride RS