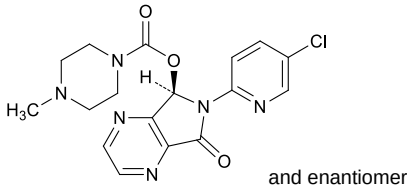
Zopiclone

ゾピクロン



and enantiomer

$C_{17}H_{17}ClN_6O_3$: 388.81

(5*RS*)-6-(5-Chloropyridin-2-yl)-7-oxo-6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyrazin-5-yl 4-methylpiperazine-1-carboxylate

[*43200-80-2*]

Zopiclone contains not less than 99.0% and not more than 101.0% of zopiclone ($C_{17}H_{17}ClN_6O_3$), calculated on the dried basis.

Description Zopiclone occurs as a white to pale yellow crystalline powder.

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

It dissolves in 0.1 mol/L hydrochloric acid TS.

It is gradually colored to pale brown by light.

A solution of Zopiclone in 0.1 mol/L hydrochloric acid TS (1 in 40) shows no optical rotation.

Melting point: 175 – 178℃

Zopiclone shows crystal polymorphism.

Identification **(1)** Determine the absorption spectrum of a solution of Zopiclone in 0.1 mol/L hydrochloric acid TS (1 in 100,000) as directed under Ultraviolet-visible Spectrophotometry <*2.24*>, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wavelengths.

(2) Determine the infrared absorption spectrum of Zopiclone as directed in the potassium bromide disk method under Infrared Spectrophotometry <*2.25*>, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers. If any difference appears between the spectra, dissolve Zopiclone in 21 times its mass of 2-propanol, heat under a reflux condenser for 15 minutes, and gradually cool to 5℃ or below. Maintain the temperature for more than 2 hours, filter this solution, wash the residue with 2-propanol, dry, and repeat the test on the residue.

Purity **(1)** Heavy metals <*1.07*>—Proceed with 2.0 g of Zopiclone according to Method 2, and perform the test. Prepare the control solution with 4.0 mL of Standard Lead Solution (not more than 20 ppm).

(2) Related substances—Conduct this procedure using light-resistant vessels. Dissolve 40 mg of Zopiclone in 100 mL of the mobile phase, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add the mobile phase to make exactly 100 mL, and use this solution as the standard solution. Perform the test with exactly 20 μL each of the sample solution and standard solution as directed under Liquid Chromatography <*2.01*> according to the following conditions, and determine each peak area by the automatic integration method: the peak areas of the related substance A having the relative retention time of about 0.1 to zopiclone, the related substance B having the relative retention time of about 0.2, the related substance C having the relative retention time of about 0.5, the related substance D having the relative retention time of about 0.9 and the peaks other than mentioned above, obtained from the sample solution, are not larger than 1/10 times the peak area of zopiclone from the standard solution. For the peak areas of the related substances A and B, multiply their relative response factors, 0.7, and 0.6, respectively.

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 303 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 30℃.

Mobile phase: Dissolve 1.20 g of sodium dihydrogen phosphate and 8.2 g of sodium lauryl sulfate in 1000 mL of water, and adjust to pH 3.5 with diluted phosphoric acid (1 in 10). To 620 mL of this solution add 380 mL of acetonitrile, and adjust to pH 4.0 with 8 mol/L sodium hydroxide TS or diluted phosphoric acid (1 in 10).

Flow rate: 1.5 mL per minute.

Time span of measurement: About 1.5 times as long as the retention time of zopiclone, beginning after the solvent peak.

System suitability—

Test for required detectability: Pipet 1 mL of the standard solution, and add the mobile phase to make exactly 20 mL. Confirm that the peak area of zopiclone obtained with 20 μL of this solution is equivalent to 3.5 to 6.5% of that with 20 μL of the standard solution.

System performance: When the procedure is run with 20 μL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of zopiclone are not less than 7500 and not more than 1.5, respectively.

System repeatability: When the test is repeated 6 times with 20 μL of the standard solution under the above

operating conditions, the relative standard deviation of the peak area of zopiclone is not more than 3.0%.

Loss on drying *<2.41>* Not more than 0.5% (2 g, in vacuum, 100℃, 24 hours).

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

Assay Weigh accurately about 0.3 g of Zopiclone, dissolve in 50 mL of a mixture of acetic anhydride and acetic acid (100) (4:1), 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
＝38.88 mg of $C_{17}H_{17}ClN_6O_3$

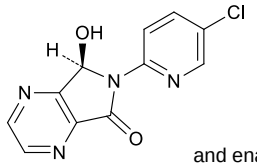
Containers and storage Containers—Well-closed containers.

Storage—Light-resistant.

Others

Related substance A:

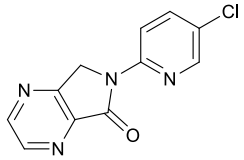
(7*RS*)-6-(5-Chloropyridin-2-yl)-7-hydroxy-6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyrazin-5-one



and enantiomer

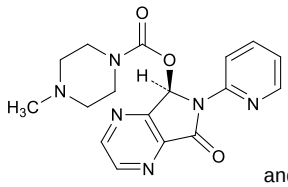
Related substance B:

6-(5-Chloropyridin-2-yl)-6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyrazin-5-one



Related substance C:

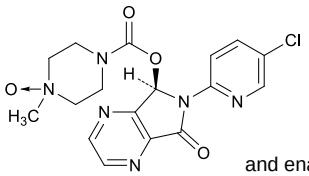
(5*RS*)-7-Oxo-6-(pyridin-2-yl)-6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyrazin-5-yl 4-methylpyperazine-1-carboxylate



and enantiomer

Related substance D:

(5*RS*)-6-(5-Chloropyridin-2-yl)-7-oxo-6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyrazin-5-yl 4-methylpyperazine-1-carboxylate 4-oxide



and enantiomer