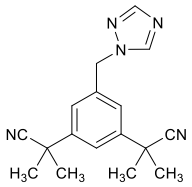
Anastrozole

アナストロゾール



$C_{17}H_{19}N_5$: 293.37

2,2'-[5-(1*H*-1,2,4-Triazol-1-ylmethyl)benzene-1,3-diyl]bis(2-methylpropanenitrile)

[*120511-73-1*]

Anastrozole contains not less than 98.0% and not more than 102.0% of anastrozole ($C_{17}H_{19}N_5$).

Description Anastrozole occurs as a white, crystalline powder or powder.

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

It shows crystal polymorphism.

Identification **(1)** Determine the absorption spectrum of a solution of Anastrozole in methanol (1 in 50,000) as directed under Ultraviolet-visible Spectrophotometry <*2.24*>, and compare the spectrum with the Reference Spectrum or the spectrum of a solution of Anastrozole 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 Anastrozole 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 Anastrozole RS: both spectra exhibit similar intensities of absorption at the same wave numbers.

Purity **(1)** Heavy metals－Being specified separately when the drug is granted approval based on the Law.

(2) Related substances－Weigh accurately about 50 mg of Anastrozole, add 10 mL of acetonitrile for liquid chromatography, sonicate to dissolve, add the mobile phase A to make exactly 25 mL, and use this solution as the sample solution. Separately, weigh accurately about 50 mg of Anastrozole RS, add 10 mL of acetonitrile, sonicate to dissolve, and add the mobile phase A to make exactly 25 mL. Pipet 1 mL of this solution, add the mobile phase A to make exactly 100 mL, and use this solution as the standard solution. Perform the test with exactly 10 μL each of the sample solution and standard solution as directed under Liquid Chromatography <*2.01*> according to the following conditions. Determine the peak area, A_T, of each related substance from the sample solution, and the peak area, A_S, of anastrozole from the standard solution by the automatic integration method, and calculate the amounts of related substances by the following equation: the amounts of the related substances A and B, having the relative retention times of about 0.63 and about 2.2 to anastrozole, obtained from the sample solution are not more than 0.2%, respectively, each of other related substances is not more than 0.1%, and the total amount of other related substances is not more than 0.2%. Furthermore, the total amount of the related substances is not more than 0.5%.

$$\text{Amount (\%) of related substance} = M_S / M_T \times A_T / A_S$$

M_S: Amount (mg) of Anastrozole RS taken

M_T: Amount (mg) of Anastrozole taken

Operating conditions－

Detector, column, column temperature, mobile phases A and B, flowing of mobile phase and flow rate: Proceed as directed in the operating conditions in the Assay.

Time span of measurement: For 40 minutes after injection of the sample solution.

System suitability－

Test for required detectability: Pipet 1 mL of the standard solution, and add the mobile phase A to make exactly 20 mL. Confirm that the peak area of anastrozole obtained with 10 μL of this solution is equivalent to 3 to 7% of that with 10 μL of the standard solution.

System performance: When the procedure is run with 10 μL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of anastrozole are not less than 1500 and not more than 1.4, respectively.

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 peak area of anastrozole is not more than 2.0%.

Water <*2.48*> Not more than 0.3% (50 mg, coulometric titration).

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

Assay Weigh accurately about 25 mg each of Anastrozole and Anastrozole RS, to each add 20 mL of acetonitrile for liquid chromatography, sonicate to dissolve, add the mobile phase A to make exactly 50 mL, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with exactly 10 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 anastrozole in each solution.

$$\text{Amount (mg) of anastrozole } (C_{17}H_{19}N_5) = M_S \times A_T / A_S$$

M_S: Amount (mg) of Anastrozole RS taken

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 215 nm).

Column: A stainless steel column 3.2 mm in inside diameter and 10 cm in length, packed with octadecylsilyl and octylsilyl groups bound porous silica gel for liquid chromatography (5 μm in particle diameter).

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

Mobile phase A: A mixture of water, methanol for liquid chromatography, acetonitrile for liquid chromatography and trifluoroacetic acid (1200:600:200:1).

Mobile phase B: A mixture of methanol for liquid chromatography, water, acetonitrile for liquid chromatography and trifluoroacetic acid (900:800:300:1).

Flowing of mobile phase: Control the gradient by mixing the mobile phases A and B as directed in the following table.

Time after injection of sample (min)	Mobile phase A (vol%)	Mobile phase B (vol%)
0 — 10	100	0
10 – 40	100 → 0	0 → 100

Flow rate: 0.75 mL per minute (the retention time of anastrozole is about 6 minutes).

System suitability—

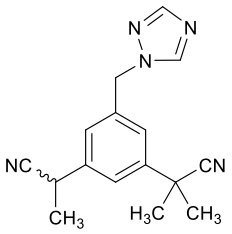
System performance: When the procedure is run with 10 μL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of anastrozole are not less than 1200 and not more than 1.4, respectively.

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 peak area of anastrozole is not more than 1.0%.

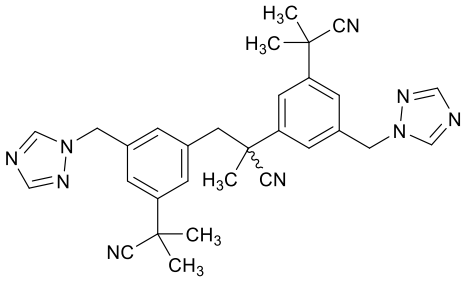
Containers and storage Containers—Tight containers.

Others

Related substance A: 2-[3-(1-Cyanoethyl)-5-(1*H*-1,2,4-triazol-1-ylmethyl)phenyl]-2-methylpropanenitrile



Related substance B: 2,3-Bis[3-(2-cyanopropan-2-yl)-5-(1*H*-1,2,4-triazol-1-ylmethyl)phenyl]-2-methylpropanenitrile



Add the following to 9.01 Reference Standards section (1):

Anastrozole RS

Add the following to 9.42 Solid Supports/Column Packings for Chromatography:

Octadecylsilyl and octylsilyl groups bound porous silica gel for liquid chromatography A porous silica gel bound with octadecylsilyl and octylsilyl groups, prepared for liquid chromatography.