

Containers and storage Containers—Well-closed containers.

Storage—Light-resistant.

Azathioprine Tablets

アザチオプリン錠

Azathioprine Tablets contain not less than 95% and not more than 105% of the labeled amount of azathioprine ($C_9H_7N_7O_2S$; 277.26).

Method of preparation Prepare as directed under Tablets, with Azathioprine.

Identification (1) Weigh a quantity of powdered Azathioprine Tablets, equivalent to 0.01 g of Azathioprine according to the labeled amount. Add 50 mL of water, shake well while warming, and filter. Proceed with 5 mL of the filtrate as directed in the Identification (1) under Azathioprine.

(2) Proceed with 1 mL of the filtrate obtained in (1) as directed in the Identification (2) under Azathioprine.

(3) Determine the absorption spectrum of the sample solution in the Assay as directed under the Ultraviolet-visible Spectrophotometry: it exhibits a maximum between 278 nm and 282 nm.

(4) Weigh a quantity of powdered Azathioprine Tablets, equivalent to 0.1 g of Azathioprine to the labeled amount. Add 10 mL of a solution of ammonia solution (28) in methanol (1 in 10), shake well, filter, and use the filtrate as the sample solution. Separately, dissolve 0.1 g of Azathioprine Reference Standard in 10 mL of a solution of ammonia solution (28) in methanol (1 in 10), and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 5 μ L each of the sample solution and the standard solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Develop the plate with a mixture of chloroform, a solution of ammonia solution (28) in methanol (1 in 10), *n*-butyl formate and 1,2-dichloroethane (15:10:5:2) to a distance of about 15 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): the spots from the sample solution and the standard solution show the same *R_f* value.

Assay Weigh accurately and powder not less than 20 Azathioprine Tablets. Weigh accurately a portion of the powder, equivalent to about 0.1 g of azathioprine ($C_9H_7N_7O_2S$), add 20 mL of dimethylsulfoxide for ultraviolet-visible spectrophotometry, shake well, add 0.1 mol/L hydrochloric acid TS to make exactly 500 mL, and filter. Discard the first 20 mL of the filtrate, measure exactly 3 mL of the subsequent filtrate, add 0.1 mol/L hydrochloric acid TS to make exactly 100 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.1 g of Azathioprine Reference Standard, previously dried at 105° C for 5 hours, dissolve in 20 mL of dimethylsulfoxide for ultraviolet-visible spectrophotometry, and add 0.1 mol/L hydrochloric acid TS to make exactly 500 mL. Measure exactly 3 mL of this solution, add 0.1 mol/L hydrochloric acid TS to make exactly 100 mL, and use this solution as the

standard solution. Determine the absorbances, A_T and A_S , of the sample solution and the standard solution at 280 nm as directed under the Ultraviolet-visible Spectrophotometry, respectively.

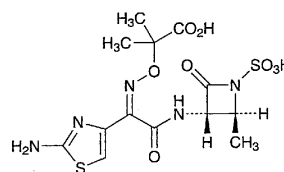
$$\begin{aligned} & \text{Amount (mg) of azathioprine (C}_9\text{H}_7\text{N}_7\text{O}_2\text{S)} \\ &= \text{amount (mg) of Azathioprine Reference Standard} \\ & \quad \times \frac{A_T}{A_S} \end{aligned}$$

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Aztreonam

アズトレオナム



$C_{13}H_{17}N_5O_8S_2$; 435.43
2-[(Z)-(2-Aminothiazol-4-yl)-[(2*S*,3*S*)-2-methyl-4-oxo-1-sulfoazetid-3-ylcarbamoyl]-methyleneaminooxy]-2-methyl-1-propanoic acid
[78110-38-0]

Aztreonam contains not less than 920 μ g (potency) per mg, calculated on the anhydrous basis. The potency of Aztreonam is expressed as mass (potency) of aztreonam ($C_{13}H_{17}N_5O_8S_2$).

Description Aztreonam occurs as a white to yellowish white crystalline powder.

It is freely soluble in dimethylsulfoxide, slightly soluble in water and in methanol, and very slightly soluble in ethanol (95).

Identification (1) Determine the absorption spectrum of a solution of Aztreonam (3 in 100,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of Aztreonam Reference Standard: both spectra exhibit similar intensities of absorption at the same wavelength.

(2) Determine the spectrum of a solution of Aztreonam in deuterated dimethylsulfoxide for nuclear magnetic resonance spectroscopy (1 in 10), using a light hydrogen substance existing in deuterated dimethylsulfoxide for nuclear magnetic resonance spectroscopy as an internal reference compound and 2.50 ppm for its chemical shift, as directed under the Nuclear Magnetic Resonance Spectroscopy (1H): it exhibits a multiple signal at around δ 1.5 ppm, and a single signal at around δ 7.0 ppm. The ratio of integrated intensity of each signal is 9:1.

Optical rotation $[\alpha]_D^{20}$: -26 – -32° (0.25 g calculated on the anhydrous bases, water, 50 mL, 100 mm).

pH Dissolve 0.05 g of Aztreonam in 10 mL of water: the pH of this solution is between 2.2 and 2.8.

Purity (1) Clarity and color of solution—Dissolve 0.1 g of Aztreonam in 20 mL of water: the solution is clear and colorless to pale yellow.

(2) Heavy metals—Proceed with 2.0 g of Aztreonam according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

(3) Arsenic—Prepare the test solution with 1.0 g of Aztreonam according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

(4) Related substances—Dissolve 0.04 g of Aztreonam in 100 mL of water, and use this solution as the sample solution. Pipet 2 mL of the sample solution, add water to make exactly 100 mL, and use this solution as the standard solution. Perform the test with 25 μ L each of these solutions as directed under the Liquid Chromatography according to the following conditions, and calculate the areas of each peak by the automatic integration method: the area of each peak is not more than the peak area of aztreonam from the standard solution, and the total area of peaks other than aztreonam from the sample solution is not more than 2.5 times of the peak area of aztreonam from the standard solution.

Operating conditions—

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

Detector: An ultraviolet absorption photometer (wavelength: 254 nm).

Time span of measurement: About 4 times as long as the retention time of aztreonam after the solvent peak.

System suitability—

Test for required detection: Pipet 5 mL of the standard solution, add water to make exactly 10 mL, and use this solution as the solution for the test for required detection. Pipet 1 mL of the solution, and add water to make exactly 10 mL. Confirm that the peak area of aztreonam obtained from 25 μ L of this solution is equivalent to 7 to 13% of that obtained from 25 μ L of the solution for the test for required detection.

System performance: When the procedure is run under the above operating conditions with 25 μ L of the standard solution obtained in the Assay, the internal standard and aztreonam 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 25 μ L of the standard solution under the above operating conditions, the relative standard deviation of the peak areas of aztreonam is not more than 2.0%.

Water Not more than 2.0% (0.5 g, volumetric titration, direct titration).

Residue on ignition Not more than 0.1% (1 g).

Assay Weigh accurately an amount of Aztreonam and Aztreonam Reference Standard, equivalent to about 0.02 g (potency), dissolve each in 70 mL of water, add exactly 10 mL of the internal standard solution and water to make 100 mL, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with 25 μ L each of these solutions as directed under the Liquid Chromatography according to the following conditions, and calculate the ratios, Q_T and Q_S , of the peak area of aztreonam to that of the internal standard of each solution.

Amount [μ g (potency)] of aztreonam ($C_{13}H_{17}N_5O_8S_2$)
= amount [mg (potency)] of Aztreonam Reference

$$\text{Standard} \times \frac{Q_T}{Q_S} \times 1000$$

Internal standard solution—A solution of 4-aminobenzoic acid (1 in 6250).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 280 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 (10 μ m in particle diameter).

Column temperature: A constant temperature of about 40°C.

Mobile phase: Dissolve 1.7 g of tetrabutylammonium hydrogensulfate in 300 mL of water, adjust to pH 3.0 with 0.5 mol/L disodium hydrogenphosphate TS, and add water to make 1000 mL. To 650 mL of this solution add 350 mL of methanol.

Flow rate: Adjust the flow rate so that the retention time of aztreonam is about 8 minutes.

System suitability—

System performance: When the procedure is run with 25 μ L of the standard solution under the above operating conditions, the internal standard and aztreonam 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 25 μ L of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of aztreonam to that of the internal standard is not more than 1.5%.

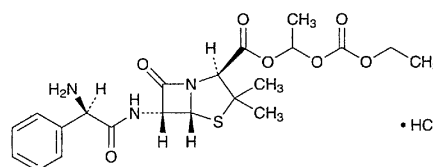
Containers and storage Containers—Tight containers.

Storage—Light-resistant.

Bacampicillin Hydrochloride

Ampicillin Ethoxycarbonyloxyethyl Hydrochloride

塩酸バカンピシリン



$C_{21}H_{27}N_3O_7S \cdot HCl$: 501.98

1-Ethoxycarbonyloxyethyl (2S,5R,6R)-6-[(2R)-2-amino-2-phenylacetylamino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate monohydrochloride [37661-08-8]

Bacampicillin Hydrochloride contains not less than 626 μ g (potency) per mg, calculated on the anhydrous basis. The potency of Bacampicillin Hydrochloride is