

trol solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

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

(5) Related substances—Dissolve 0.05 g of Allopurinol in 10 mL of ammonia TS, and use this solution as the sample solution. Pipet 1 mL of this solution, add ammonia TS to make exactly 200 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 5  $\mu$ L each of the sample solution and the standard solution on a plate of cellulose with fluorescent indicator for thin-layer chromatography. Develop the plate with ammonia TS-saturated 1-butanol to a distance of about 10 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution.

**Loss on drying** Not more than 0.5% (1 g, 105°C, 4 hours).

**Residue on ignition** Not more than 0.10% (1 g).

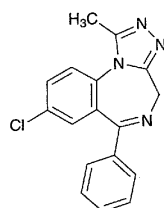
**Assay** Weigh accurately about 0.16 g of Allopurinol, previously dried, dissolve in 70 mL of *N,N*-dimethylformamide by warming. Cool, and titrate with 0.1 mol/L tetramethylammonium hydroxide VS (potentiometric titration). To 70 mL of *N,N*-dimethylformamide add 12 mL of water, perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L tetramethylammonium hydroxide VS  
= 13.611 mg of C<sub>5</sub>H<sub>4</sub>N<sub>4</sub>O

**Containers and storage** Containers—Tight containers.

## Alprazolam

アルプラゾラム



C<sub>17</sub>H<sub>13</sub>ClN<sub>4</sub>: 308.76  
8-Chloro-1-methyl-6-phenyl-4H-[1,2,4]triazolo[4,3-*a*][1,4]benzodiazepine [28981-97-7]

Alprazolam, when dried, contains not less than 98.5% of C<sub>17</sub>H<sub>13</sub>ClN<sub>4</sub>.

**Description** Alprazolam occurs as white crystals or crystalline powder.

It is freely soluble in chloroform, soluble in methanol and in ethanol (95), sparingly soluble in acetic anhydride, and practically insoluble in water.

It dissolves in dilute nitric acid.

**Identification** (1) Determine the absorption spectrum of a solution of Alprazolam in ethanol (95) (1 in 200,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wavelength.

(2) Dissolve 0.05 g of Alprazolam in 0.7 mL of deuteriochloroform for nuclear magnetic resonance spectroscopy, and determine the spectrum of this solution using tetramethylsilane for nuclear magnetic resonance spectroscopy as an internal reference compound, as directed under the Nuclear Magnetic Resonance Spectroscopy (<sup>1</sup>H): it exhibits a single signal A at around  $\delta$  2.6 ppm, doublet signals B and C at around  $\delta$  4.0 ppm and  $\delta$  5.4 ppm, and a broad signal D between  $\delta$  7.1 ppm and 7.9 ppm. The ratio of integrated intensity of each signal, A:B:C:D, is about 3:1:1:8.

(3) Perform the test with Alprazolam as directed under the Flame Coloration Test (2): a green color appears.

**Melting point** 228 – 232°C

**Purity** (1) Chloride—Dissolve 0.5 g of Alprazolam in 10 mL of dilute nitric acid, and add water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution with 0.20 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.014%).

(2) Heavy metals—Proceed with 2.0 g of Alprazolam according to Method 4, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

(3) Related substances—Dissolve 0.050 g of Alprazolam in 10 mL of methanol, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add methanol to make exactly 100 mL, then pipet 1 mL of this solution, add methanol to make exactly 10 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 20  $\mu$ L each of the sample solution and the standard solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Develop with a mixture of acetone, hexane, ethyl acetate and ethanol (95) (4:2:2:1) to a distance of about 10 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution.

**Loss on drying** Not more than 0.5% (1 g, reduced pressure not exceeding 0.67 kPa, 60°C, 4 hours).

**Residue on ignition** Not more than 0.10% (1 g).

**Assay** Weigh accurately about 0.25 g of Alprazolam, previously dried, dissolve in 100 mL of acetic anhydride, and titrate 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  
= 15.438 mg of C<sub>17</sub>H<sub>13</sub>ClN<sub>4</sub>

**Containers and storage** Containers—Well-closed containers.