Edition: BP 2025 (Ph. Eur. 11.6 update)

Tioguanine Tablets

General Notices

Action and use

Purine analogue; cytostatic.

DEFINITION

Tioguanine Tablets contain Tioguanine.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of tioguanine, $C_5H_5N_5S$

92.5 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of the powdered tablets containing 0.5 g of Tioguanine with 10 mL of 1M *sodium hydroxide* and filter. Acidify the filtrate with *hydrochloric acid*, filter, dissolve the precipitate in 13.5M *ammonia*, evaporate to dryness and dry the residue at 105° at a pressure not exceeding 0.7 kPa for 5 hours. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of tioguanine (*RS 340*).

TESTS

Dissolution

Comply with the requirements for Monographs of the British Pharmacopoeia in the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 50 revolutions per minute.
(b) Use 900 mL of *water* at a temperature of 37°, as the medium.

PROCEDURE

(1) After 45 minutes withdraw 10 mL of the medium and filter. To 2 mL of the filtrate add 2 mL of 1M *hydrochloric acid* and dilute to 20 mL with *water*. Measure the *absorbance* of the solution at the maximum at 348 nm, Appendix II B, using 0.1M *hydrochloric acid* in the reference cell.
(2) Measure the *absorbance* of a suitable solution of *tioguanine BPCRS* using 0.1M *hydrochloric acid* in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of tioguanine, $C_5H_5N_5S$, in the medium from the absorbances obtained and using the declared content of $C_5H_5N_5S$ in *tioguanine BPCRS*.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Disperse a quantity of the powdered tablets containing 40 mg of Tioguanine in 100 mL of 0.01M *sodium hydroxide* with the aid of ultrasound for 5 minutes. Mix and filter. Dilute 1 volume of the filtrate to 2 volumes with mobile phase.
(2) Dilute 1 volume of solution (1) to 100 volumes with a mixture of 1 volume of 0.01M *sodium hydroxide* and 9 volumes of mobile phase. Further dilute 1 volume of this solution to 5 volumes with the same solvent mixture.
(3) Dissolve 16 mg of *guanine BPCRS* in 100 mL of 0.01M *sodium hydroxide* and dilute 1 volume of the resulting solution to 20 volumes with the mobile phase.
(4) Dissolve 40 mg each of *tioguanine BPCRS* and *guanine BPCRS* in 100 mL of 0.01M *sodium hydroxide* and dilute 1 volume of this solution to 10 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (5 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Waters Atlantis dC18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 248 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

0.05M *anhydrous sodium dihydrogen orthophosphate* adjusted to pH 3.0 with *orthophosphoric acid (85%)*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution factor* between the peaks due to tioguanine and guanine is at least 3.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to guanine is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (4%);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of the areas of any other *secondary peaks* is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%).

Disregard any peak with an area less than 0.25 times the area of the principal peak in the chromatogram obtained with solution (2) (0.05%).

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) To a quantity of the powdered tablets containing 40 mg of Tioguanine add 70 mL of 0.01M *sodium hydroxide*, shake for 15 minutes and dilute to 100 mL with the same solvent. Filter and dilute 1 volume of the resulting solution to 10 volumes with the mobile phase.
(2) Dissolve 40 mg of *tioguanine BPCRS* in 100 mL of 0.01M *sodium hydroxide* and dilute 1 volume of the resulting solution to 10 volumes with the mobile phase.
(3) Dissolve 40 mg each of *tioguanine BPCRS* and *guanine BPCRS* in 100 mL of 0.01M *sodium hydroxide* and dilute 1 volume of the resulting solution to 10 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution factor* between the peaks due to tioguanine and guanine is at least 3.0.

DETERMINATION OF CONTENT

Calculate the content of $C_5H_5N_5S$ in the tablets from the chromatograms obtained and using the declared content of $C_5H_5N_5S$ in *tioguanine BPCRS*.