Protionamide tablets (Protionamidi compressi)

2018-01

Category. Tuberculostatic.

Storage. Protionamide tablets should be kept in a well-closed container, protected from light.

Additional information. Strength in the current WHO Model List of Essential Medicines (EML): 125 mg; 250 mg. Strength in the current WHO EML for children: 125 mg; 250 mg.

Requirements

Comply with the monograph for *Tablets*.

Definition. Protionamide tablets contain not less than 90.0% and not more than 110.0% of the amount of protionamide ($C_9H_{12}N_2S$) stated on the label.

Identity tests

-Either test A alone or tests B and C may be applied.

A. Extract a quantity of the powdered tablets containing about 25 mg of protionamide with 5 mL of methanol R, filter and evaporate the filtrate to dryness. Carry out the examination as described under *1.7 Spectrophotometry in the infrared region*. The infrared absorption spectrum is concordant with the spectrum obtained from protionamide RS or with the reference spectrum of protionamide.

If the spectra thus obtained are not concordant repeat the test using the residues obtained by separately dissolving the test substance and protionamide RS in a small amount of methanol R and evaporating to dryness. The infrared absorption spectrum is concordant with the spectrum obtained from protionamide RS.

B. To a quantity of powdered tablets containing the equivalent of about 2.5 mg of protionamide add 25 mL ethanol (~750 g/L) TS, shake and filter. Dilute 1 mL of the filtrate to 10 mL with the same solvent. The absorption spectrum *(1.6)* of the resulting solution, when observed between 230 nm and 350 nm, exhibits a maximum at about 291 nm and a minimum at about 256 nm.

C. Carry out the test as described under *1.14.1 Chromatography*, High-performance liquid chromatography using the conditions given under “Assay”. The retention time of the principal peak in the chromatogram obtained from solution (1) corresponds to the retention time of the peak due to protionamide in the chromatogram obtained with solution (2).

Dissolution. Carry out the test as described under *5.5 Dissolution test for solid oral dosage forms*, using as the dissolution medium 900 mL of hydrochloric acid (~4 g/L) TS and rotating the paddle at 50 revolutions per minute. At 30 minutes withdraw a sample of 10 mL of the medium through an in-line filter and allow the filtered sample to cool to room temperature. Measure the absorbance *(1.6)* of a 1 cm layer of the resulting solution, suitably diluted if necessary, at a wavelength of 277 nm using the dissolution medium as the blank. Measure at the same time and under the same conditions the absorbance of a suitable solution of protionamide RS in the dissolution medium.

For each of the tablets tested, calculate the total amount of protionamide ($C_9H_{12}N_2S$) in the dissolution medium from the absorbances obtained. Evaluate the results as described under *5.5 Dissolution test for solid dosage forms*. The amount of protionamide in solution for each tablet is not less than 75% (Q) of the amount stated on the label.

*[**Note from the Secretariat**. It is intended to determine the absorptivity value of protionamide during the establishment of protionamide RS. The value will then be included in the test description.]*

Related substances. Carry out the test as described under *1.14.1 Chromatography*, High-performance liquid chromatography using the conditions given under “Assay”.

For solution (1) transfer a quantity of the powdered tablets equivalent to 250 mg of protionamide into a 250 mL volumetric flask, disperse in 100 mL, shake vigorously and dilute to volume. Filter the resulting solution and dilute 25.0 mL of this solution to 50.0 mL. For solution (2) dilute 1 volume of solution (1) to 100 volumes with mobile phase. For solution (3) use a solution containing 0.05 mg of protionamide RS and 0.01 mg of ethionamide R per mL of mobile phase.

Inject 20 µL of solution (3). Ethionamide is eluted at a relative retention of about 0.6 with reference to protionamide (retention time about 10 minutes).The test is not valid unless the resolution between the peaks due to ethionamide and protionamide is at least 5.0.

Inject alternately 20 µL of each of solution (1) and (2). Record the chromatograms for 2 times the retention time of protionamide.

In the chromatogram obtained with solution (1):

· the area of any impurity peak is not greater than the area of the peak due to protionamide in the chromatogram obtained with solution (2) (0.5%).

Assay. Carry out the test as described under *1.14.1 Chromatography*, High-performance liquid chromatography using a stainless steel column (25 cm ×4.6 mm) packed with particles of silica gel, the surface of which has been modified with chemically-bonded octadecylsilyl groups (5 µm).

Prepare a buffer solution by mixing 2.0 mL of triethylamine R with 1000 mL water and adjusting the pH to 6.0 with phosphoric acid (~105 g/L) TS. As the mobile phase use a mixture of 72 volumes of the buffer solution and 28 volumes of acetonitrile R.

Operate with a flow rate of 1.0 mL per minute. As a detector use an ultraviolet spectrophotometer set at a wavelength of about 290 nm.

Prepare the following solutions in mobile phase. For solution (1) weigh and powder 20 tablets. Transfer a quantity of the powdered tablets containing 250.0 mg of protionamide into a 250 mL volumetric flask, disperse in 100 mL, shake vigorously and dilute to volume. Filter the resulting solution and dilute 10.0 mL of this solution to 200.0 mL. For solution (2) dilute 25.0 mg of protionamide RS and 5.0 mg of ethionamide R in 50.0 mL. Dilute 10.0 mL of this solution to 100.0 mL.

Inject 20 µL of solution (2). Ethionamide is eluted at a relative retention of about 0.6 with reference to protionamide (retention time about 10 minutes).The test is not valid unless the resolution between the peaks due to ethionamide and protionamide is at least 5.0.

Inject alternately 20 µL each of solution (1) and (2). Record the chromatograms.

Measure the areas of the peaks corresponding to protionamide obtained in the chromatograms of solutions (1) and (2) and calculate the percentage content of protionamide ($C_9H_{12}N_2S$) in the tablets, using the declared content of protionamide ($C_9H_{12}N_2S$) in protionamide RS.

Impurities

The impurities limited by the requirements of this monograph include the impurity listed in the monograph on Protionamide.