Pyrazinamide tablets (Pyrazinamidi compressi)

Category. Antituberculosis drug.

Additional information. Strengths in the current WHO Model list of essential medicines: 400 mg and 150 mg (scored or dispersible tablet). Strengths in the current WHO Model list of essential medicines for children: 400 mg and 150 mg (scored or dispersible tablet). Additional available strength: 500 mg.

Requirements

Comply with the monograph for *Tablets*

Pyrazinamide tablets contain not less than 93.0% and not more than 107.0% of the amount of $C_5H_5N_3O$ stated on the label.

Identity tests

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

A. Shake a quantity of the powdered tablets equivalent to 0.25 g of Pyrazinamide with 20 mL of dehydrated ethanol R, filter and evaporate the filtrate to dryness. Dry the residue at 105 °C for 30 minutes and carry out the examination as described under *1.7 Spectrophotometry in the infrared region*. The infrared absorption spectrum of the residue is concordant with the spectrum obtained from pyrazinamide RS or with the *reference spectrum* of pyrazinamide.

B. Shake a quantity of the powdered tablets equivalent to 0.050 g of Pyrazinamide with 50 mL of water and filter. Dilute 1 mL of the filtrate to 100 mL with water. The absorption spectrum of this solution, when observed between 230 nm and 350 nm, exhibits two maxima at about 268 nm and 310 nm. The ratio of the absorbance of a 1 cm layer at 268 nm to that at 310 nm is between 11.6 and 12.0.

C. To a quantity of the powdered tablets equivalent to 0.06 g of Pyrazinamide add 5 mL of sodium hydroxide (~80 g/l) TS and heat on a water-bath; vapours are evolved. Insert moistened pH-indicator paper R into the vapours; the colour of the paper changes to an alkaline range, and an odour of ammonia is perceptible.

Related substances

Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography using silica gel R4 as the coating substance and a mixture of 6 volumes of 1-butanol R, 2 volumes of glacial acetic acid R and 2 volumes of water as the mobile phase, but allowing the solvent front to ascend 10 cm above the line of application. Apply separately to the plate 20 µl of each of the following two solutions. For solution (A) shake a quantity of the powdered tablets equivalent to 0.1 g of Pyrazinamide with 50 mL of a mixture of 9 volumes of chloroform R and 1 volume of methanol R and filter. Evaporate the filtrate to dryness and dissolve the residue in sufficient mixture of solvents to produce 10 mL. For solution (B) dilute 1 volume of solution A to 500 volumes with the same mixture of solvents. After removing the plate from the chromatographic chamber allow it to dry in air and examine the chromatogram immediately in ultraviolet light (254 nm).

Any spot obtained with solution A, other than the principal spot, is not more intense than that obtained with solution B.

Assay

Weigh and powder 20 tablets. Add a quantity of the powder equivalent to about 0.1 g of Pyrazinamide, accurately weighed, to 200 mL of water, allow to stand for 10 minutes, swirling occasionally, mix in an ultrasonic bath for 10 minutes and dilute to 500 mL with water. Filter and discard the first 20 mL of filtrate. Dilute 5 mL of the filtrate to 100 mL with water.

Measure the absorbance of this solution in a 1 cm layer at the maximum at about 268 nm. Calculate the content of $C_5H_5N_3O$, using the absorptivity value of 65.0 ($A^{1\%}_{1cm}$ = 650).

Dissolution/Disintegration

-Either test A or test B may be applied

A. **Dissolution.** Carry out the test as described under *5.5 Dissolution test for solid oral dosage forms* using as the dissolution medium 500 mL of dissolution buffer pH 6.8, TS and rotating the paddle at 75 revolutions per minute. At 30 minutes withdraw a sample of 10 mL of the medium through an in-line filter. Measure the *absorbance (1.6)* of a 1 cm layer of the filtered sample, suitably diluted if necessary, at the maximum at about 268 nm. At the same time measure the absorbance at the maximum at about 268 nm of a suitable solution of pyrazinamide RS in dissolution buffer pH 6.8 TS using the same buffer as the blank.

For each of the six tablets tested calculate the total amount of pyrazinamide ($C_5H_5N_3O$) in the medium. The amount in solution for each tablet is not less than 80% of the amount declared on the label. If the amount obtained for one of the six tablets is less than 80% repeat the test using a further six tablets; the average amount for all 12

tablets tested is not less than 75% and the amount obtained for no tablet is less than 60%.

B. **Disintegration.** Comply with *5.3 Disintegration test for tablets and capsules* operating the apparatus for 10 minutes. If the tablets do not comply carry out test A above.