Ethambutol hydrochloride tablets (Ethambutoli hydrochloridi compressi)

Category. Antituberculosis drug.

Storage. Ethambutol hydrochloride tablets should be kept in a tightly closed container.

Additional information. Strengths in the current WHO Model list of essential medicines: 100, 400 mg. Strengths in the current WHO Model list of essential medicines for children: 100, 400 mg.

Requirements

Comply with the monograph for "Tablets".

Definition. Ethambutol hydrochloride tablets contain Ethambutol hydrochloride. They contain not less than 90.0% and not more than 110.0% of the amount of ethambutol hydrochloride ($C_{10}H_{24}N_2O_2$, 2HCl) stated on the label.

Identity tests

• Either tests A, B and D or tests C and D may be applied.

A. Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography, using silica gel R1 as the coating substance and a mixture of 100 volumes of methanol R and 1.5 volumes of ammonia (~260 g/l) TS as the mobile phase. Apply separately to the plate 10 µl of each of the following two solutions. For solution (A) shake a quantity of the powdered tablets containing about 10 mg of Ethambutol hydrochloride with 10 mL of methanol R, filter, and use the filtrate. For solution (B) use 1.0 mg of ethambutol hydrochloride RS per mL of methanol R. After removing the plate from the chromatographic chamber, allow it to dry in air, and expose it to the vapour of iodine R until spots appear. Examine the chromatogram in daylight.

The principal spot obtained with solution A corresponds in position, appearance and intensity to that obtained with solution B.

B. See the test described under Assay. The retention time of the principal peak in the chromatogram obtained with solution (1) corresponds to that of the principal peak in the chromatogram obtained with solution (2).

To a quantity of the powdered tablets containing about 0.1 g of Ethambutol hydrochloride add 10 mL of methanol R and shake. Filter and evaporate the filtrate to dryness. Use the residue for tests C and D.

C. Carry out the examination with the residue as described under 1.7 Spectrophotometry in the infrared region. The infrared absorption spectrum is concordant with the spectrum obtained from ethambutol hydrochloride RS or with the *reference spectrum* of ethambutol hydrochloride.

D. The residue yields reaction A described under 2.1 General identification tests as characteristic of chlorides.

2-Aminobutanol. Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography, using silica gel R1 as the coating substance and a mixture of 11 volumes of ethyl acetate R, 7 volumes of glacial acetic acid R, 1 volume of hydrochloric acid (~420 g/l) TS, and 1 volumes of water R as the mobile phase. Apply separately to the plate 2 µl of each of the following two solutions. For solution (A) shake a quantity of the powdered tablets containing about 0.5 g of Ethambutol hydrochloride with 10 mL of methanol R for 5 minutes, filter, and use the filtrate. For solution (B) use 0.5 mg of 2-aminobutanol R per mL of methanol R. After removing the plate from the chromatographic chamber, allow it to dry in air, heat at 105°C for 5 minutes, cool, spray with triketohydrindene/cadmium TS, and heat again at 90°C for 5 minutes. Examine the chromatogram in daylight.

Any spot corresponding to 2-aminobutanol obtained with solution A is not more intense than that obtained with solution B (1.0%).

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. Allow the filtered sample to cool to room temperature and dilute if necessary [solution (3)]. Determine the content of ethambutol hydrochloride ($C_{10}H_{24}N_2O_2$, 2HCl) as described under Assay using solution (3) in place of solution (1).

For each of the six tablets tested, calculate the total amount of ethambutol hydrochloride, ($C_{10}H_{24}N_2O_2$, 2HCl) in the medium from the results obtained. The amount in solution for each tablet is not less than 80% of the amount stated 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.

Assay

Determine by *1.14.1 Chromatography*, High-performance liquid chromatography, using a stainless steel column (15 cm x 4.6 mm) packed with particles of silica gel, the surface of which has been modified with chemically bonded octadecylsilyl groups, (5 µm). As the mobile phase, use a solution prepared as follows: dissolve 50 g of ammonium acetate R and 0.2 g of copper(II) acetate R in 1000 mL of water R and adjust to pH 5.0 with glacial acetic acid R. Mix 940 mL of this solution with 60 mL of methanol R.

Prepare the following solutions in water R. For solution (1) weigh and powder 20 tablets. Transfer a quantity of the powder containing about 100 mg of Ethambutol hydrochloride, accurately weighed, to a 500-mL volumetric flask. Dissolve in about 400 mL of water R by shaking for about 15 minutes. [If foaming occurs, use 400 mL of a 4% solution of methanol R in place of the water.] Dilute to 500 mL with water R. Filter a portion of this solution through a 0.45-µm filter, discarding the first few mL of the filtrate. For solution (2) dissolve 20 mg of ethambutol hydrochloride RS in 100 mL of water R.

Operate with a flow rate of 2.0 mL per minute. As a detector use an ultraviolet spectrophotometer set at a wavelength of about 270 nm.

Inject alternately 20 µl each of solutions (1) and (2). (The peak for ethambutol hydrochloride is eluted at a retention time of approximately 6 minutes).

Measure the areas of the peak responses obtained in the chromatograms from solutions (1) and (2), and calculate the content of ethambutol hydrochloride ($C_{10}H_{24}N_2O_2$, 2HCl) from the declared content of $C_{10}H_{24}N_2O_2$, 2HCl in ethambutol hydrochloride RS.