Isoniazid tablets (Isoniazidi compressi)

**Category.** Antituberculosis drug.

**Additional information.** Strength in the current WHO Model list of essential medicines: 100 - 300mg.

**Requirements**

Comply with the monograph for "Tablets".

Isoniazid tablets contain not less than 90.0% and not more than 110.0% of the amount of C₆H₇N₃O stated on the label.

**Identity tests**

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

  A. To a quantity of the powdered tablets equivalent to about 0.1g of Isoniazid add 10ml of ethanol (~750g/l) TS and shake for 15 minutes. Centrifuge and decant the supernatant liquid. Extract the remaining liquid with two further 10-mL quantities of ethanol (~750g/l) TS and evaporate the combined extracts to dryness. 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 isoniazid RS or with the reference spectrum of isoniazid.

  B. To a quantity of the powdered tablets equivalent to about 0.1g of Isoniazid add 2.0ml of water, shake, and filter. Then add a mixture composed of 1.0ml of silver nitrate (40g/l) TS and 1.0ml of ammonia (~100g/l) TS; bubbles of nitrogen evolve, the mixture turns from yellow to black and a metallic silver mirror appears on the sides of the test-tube.

  C. To a quantity of the powdered tablets equivalent to about 1mg of Isoniazid add 50ml of ethanol (~750g/l) TS, shake, and filter. To 5ml of the filtrate add 0.1g of sodium tetraborate R and 5ml of 1-chloro-2,4 dinitrobenzene/ethanol TS, evaporate to dryness on a water-bath, and continue heating for a further 10 minutes. To the residue add 10ml of methanol R and mix; a reddish violet colour is produced.

**Related substances.** Carry out the test as described under 1.14.1 Thin-layer chromatography, using silica gel R2 as the coating substance and a mixture of 5 volumes of ethyl acetate R, 2 volumes of acetone R, 2 volumes of methanol R, and 1 volume of water as the mobile phase. Apply separately to the plate 10 μl of each of the 3 following solutions. For solution (A) shake a quantity of the powdered tablets equivalent to about 0.1g of Isoniazid with 10ml of methanol R, filter, and use the filtrate. For solution (B) use 10mg of isoniazid RS per mL of methanol R. For solution (C) dilute 1 volume of solution A to 100 volumes with methanol R. After removing the plate from the chromatographic chamber, allow it to dry in air, and examine the chromatogram in ultraviolet light (254nm).

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

**Assay.** Weigh and powder 20 tablets. Dissolve a quantity of the powdered tablets equivalent to about 0.4g of Isoniazid as completely as possible in water, filter, and wash the residue with sufficient water to produce 250ml. Place 50ml of the resulting solution in a titration vessel, add 50ml of water, 20ml of hydrochloric acid (~250g/l) TS, and 0.2g of potassium bromide R, and titrate with potassium bromate (0.0167mol/l) VS as described under 2.7 Nitrite titration.

Each mL of potassium bromate (0.0167mol/l) VS is equivalent to 3.429mg of C₆H₇N₃O.

**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 263 nm. At the same time measure the absorbance at the maximum at about 263 nm of a suitable solution of isoniazid 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 isoniazid (C₆H₇N₃O) 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.