Metronidazole tablets (Metronidazoli compressi)

Category. Anti-amoebic drug; antibacterial drug.

Additional information. Strength in the current WHO Model list of essential medicines: 200-500 mg.

Requirements

Comply with the monograph for "Tablets".

Definition. Metronidazole tablets may be film-coated and not necessarily circular in shape.

Metronidazole tablets contain not less than **95.0%** and not more than **105.0%** of the amount of $C_6H_9N_3O_3$ stated on the label.

Identity tests

To a quantity of the powdered tablets equivalent to 60 mg of Metronidazole add 20 mL of water, shake, and filter. Evaporate the filtrate to a smaller volume, allow to crystallize, separate the crystals, dry at 105 °C for 1 hour, and use the dried material for tests A and B.

A. Dissolve 20 mg of the dried material in 100 mL of a mixture of solvents composed of 1 mL of sulfuric acid (~1760 g/l) TS in 350 mL of methanol R. Further dilute 1 mL of this solution to 10 mL using the same mixture of solvents. The absorption spectrum, when observed between 220 nm and 350 nm, is qualitatively similar to that of a 20 µg/mL solution of metronidazole RS in the same mixture of solvents.

B. To 25 mg of the dried material add 0.05 g of 4-dimethylaminobenzaldehyde R dissolved in 2 mL of hydrochloric acid (~70 g/l) TS; a yellowish colour is produced. Add 0.05 g of zinc R powder; the colour changes to red-orange.

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 acetone R 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 equivalent to 0.2 g of Metronidazole with 5 mL of a mixture of equal volumes of methanol R and chloroform R for 5 minutes, filter, and use the clear filtrate. For solution (B) dissolve 20 mg of 2-methyl-5-nitroimidazole R in 10 mL of the same mixture of solvents. After removing the plate from the chromatographic chamber, allow it to dry in air, and examine the chromatogram in ultraviolet light (254 nm).

The spot obtained with solution B is more intense than any corresponding spot obtained with solution A.

Assay. Weigh and powder 20 tablets. Transfer a quantity of the powder, equivalent to about 0.2 g of Metronidazole, accurately weighed, to a sintered-glass filtering crucible, and extract with 6 quantities, each of 10 mL, of hot acetone R. Cool, add to the combined extracts 50 mL of acetic anhydride R and 0.1 mL of brilliant green/acetic acid TS, and titrate with perchloric acid (0.1 mol/l) VS as described under 2.6 Non-aqueous titration, Method A. Repeat the procedure without the powdered tablets being examined and make any necessary corrections.

Each mL of perchloric acid (0.1 mol/l) VS is equivalent to 17.12 mg of $C_6H_9N_3O_3$.

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 319 nm. At the same time measure the absorbance at the maximum at about 319 nm of a suitable solution of metronidazole 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 metronidazole ($C_6H_9N_3O_3$) 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.