

Mebendazole chewable tablets (Mebendazoli compressi manducabili)

2017-01

Category. Anthelmintic.**Storage.** Mebendazole chewable tablets should be kept in a tightly closed container.**Labelling.** The designation on the container should state that the tablets may be chewed, swallowed whole, crushed and mixed with food or liquid or dispersed in water.**Additional information.** Strengths in the current WHO Model List of Essential Medicines (EML): 100 mg, 500 mg. Strengths in the current WHO EML for children: 100 mg, 500 mg.**Requirements**Comply with the monograph for [Tablets](#).**Definition.** Mebendazole chewable tablets contain Mebendazole in a suitable basis that may contain suitable flavouring agents. Mebendazole chewable tablets contain not less than 90.0% and not more than 110.0% of the amount of mebendazole ($C_{16}H_{13}N_3O_3$) stated on the label.**Manufacture.** The formulation, manufacturing process and product packaging of Mebendazole chewable tablets are designed and controlled so as to minimize the conversion of the polymorphic form of mebendazole from C to A. They ensure that, at any stage of the life cycle of the product, when tested by a suitable method such as infrared spectrometry (see Identity test A) or X-ray powder diffractometry, the mebendazole in the tablets is predominantly in the form of polymorph C.**Identity tests**

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

A. To a quantity of the powdered tablets containing 0.05 g of Mebendazole add 20 mL of water R, shake, filter and wash the residue with three quantities, each of 10 mL of water R. Dry the residue overnight under vacuum at room temperature and carry out the examination with the residue as described under [1.7 Spectrophotometry in the infrared region](#). The two infrared absorption bands at about 3405 cm^{-1} and 1720 cm^{-1} are concordant with those in the spectrum obtained from mebendazole RS (containing mebendazole polymorph C).

B. Carry out the test as described under [1.14.1 Chromatography, Thin-layer chromatography](#) using silica gel R6 as the coating substance and a mixture of 85 volumes of dichloromethane R, 5 volumes of methanol R, 5 volumes of acetone R and 5 volumes of anhydrous formic acid R as the mobile phase. Apply separately to the plate 5 μL of each of the following solutions. For solution (A) add 2 mL of formic acid R to a quantity of the powdered tablets containing 20 mg of mebendazole and sonicate for about 5 minutes. Add 18 mL of acetone R, mix, filter and use the filtrate. For solution (B) dissolve 10 mg of mebendazole RS in 1 mL of formic acid R and shake. Add 9 mL of acetone R and mix. After removing the plate from the chromatographic chamber allow it to dry in air and examine the chromatogram in ultraviolet light (254 nm).

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

C. Carry out the test as described under [1.14.1 Chromatography, High-performance liquid chromatography](#) using the conditions under "Assay". The retention time of the principal peak in the chromatogram obtained with solution (1) corresponds to the retention time of the peak due to mebendazole obtained with solution (2).

Related substances

Carry out the test as described under [1.14.1 Chromatography, High-performance liquid chromatography](#) using a stainless steel column (10 cm \times 4.6 mm) packed with base-deactivated particles of silica gel, the surface of which has been modified with chemically-bonded octadecylsilyl groups (3 μm).

Use the following conditions for gradient elution:

mobile phase A: 7.5 g/L solution of ammonium acetate R;

mobile phase B: Acetonitrile R.

Time (min)	Mobile phase A (%v/v)	Mobile phase B (%v/v)	Comments
0–15	80 to 70	20 to 30	Linear gradient
15–20	70 to 10	30 to 90	Linear gradient
20–25	10	90	Isocratic
25–26	10 to 80	90 to 20	Return to initial composition

20–30	80	20	Isocratic re-equilibration
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Operate with a flow rate of 1.2 mL per minute. As a detector use an ultraviolet spectrophotometer set at a wavelength of 250 nm. Maintain the column temperature at 40 °C.

Prepare as a solvent a mixture of 60 volumes of methanol R and 40 volumes of water R.

For solution (1) transfer a quantity of the powdered tablets, containing about 100 mg of mebendazole, accurately weighed, to a 100 mL volumetric flask. Add 30 mL of anhydrous formic acid R and sonicate for about 20 minutes. Dilute to volume with the solvent mixture, mix and filter. For solution (2) dilute 1.0 mL of solution (1) to 100.0 mL with the solvent mixture. Dilute 5.0 mL of this solution to 20.0 mL with the solvent mixture. For solution (3) transfer 10 mg mebendazole R to a 10 mL volumetric flask, add 5 mL of methanol R and 1 mL of sodium hydroxide (~40 g/L) TS solution, heat in a water bath at 60 °C for 1 hour, cool to room temperature and adjust the solution to pH 7 with hydrochloric acid (~36.5 g/L) TS. Dilute with methanol R to volume and mix.

Inject 10 µL of solution (3). Use the chromatogram to identify the peak due to impurity A. The impurity is eluted at the relative retention of 0.4 with reference to mebendazole (retention time about 12 minutes).

The test is not valid unless in the chromatogram obtained with solution (3) the resolution between mebendazole and impurity A is at least 10.

Inject alternately 10 µL each of solution (1) and (2).

In the chromatogram obtained with solution (1):

- the area of any peak corresponding to impurity A is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.25%).

Dissolution

For 100 mg tablets. Carry out the test as described under [5.5 Dissolution test for solid oral dosage forms](#) using 900 mL of hydrochloric acid (~3.65 g/L) TS as the dissolution medium and rotating the paddle at 75 revolutions per minute. At 120 minutes withdraw a sample of 10 mL of the dissolution medium through an in-line filter. Allow the filtered sample to cool to room temperature. Dilute 5.0 mL of the filtrate to 50.0 mL with the dissolution medium.

Determine the content of mebendazole ($C_{16}H_{13}N_3O_3$) in the medium by [1.14.1 Chromatography, High-performance liquid chromatography](#) using the conditions described under “Assay” and a suitable solution of mebendazole RS as a reference solution.

For each of the tablets tested calculate the total amount of mebendazole ($C_{16}H_{13}N_3O_3$) in the medium using the declared content of $C_{16}H_{13}N_3O_3$ in mebendazole RS. The amount in solution for each tablet is not less than 60% (Q) of the amount declared on the label.

For 500 mg tablets. Carry out the test as described under [5.5 Dissolution test for solid oral dosage forms](#) using 900 mL of a 1.0% solution of sodium dodecyl sulfate R in hydrochloric acid (~0.365 g/L) TS as the dissolution medium and rotating the paddle at 75 revolutions per minute. At 60 minutes withdraw a sample of 10 mL of the dissolution medium through an in-line filter. Allow the filtered sample to cool to room temperature. Dilute 1.0 mL of the filtrate to 50.0 mL with the dissolution medium.

Determine the content of mebendazole ($C_{16}H_{13}N_3O_3$) in the medium by [1.14.1 Chromatography, High-performance liquid chromatography](#) using the conditions described under “Assay” and a suitable solution of mebendazole RS as a reference solution.

For each of the tablets tested calculate the total amount of mebendazole ($C_{16}H_{13}N_3O_3$) in the medium using the declared content of $C_{16}H_{13}N_3O_3$ in mebendazole RS. The amount in solution for each tablet is not less than 70% (Q) of the amount declared on the label.

Assay

Carry out the test as described under [1.14.1 Chromatography, High-performance liquid chromatography](#) using a stainless steel column (10 cm × 4.6 mm) packed with octadecylsilyl base-deactivated silica gel for chromatography R (3 µm).

As the mobile phase use a solution prepared as follows: dissolve 7.5 g of ammonium acetate R in 1000 mL of water R, mix and filter. Mix 750 mL of this solution with 250 mL of acetonitrile R.

Prepare as a solvent a mixture of 60 volumes of methanol R and 40 volumes of water R.

Prepare the following solutions. For solution (1) weigh and powder 20 tablets. Transfer a quantity of the powdered tablets, containing about 100 mg of mebendazole, accurately weighed, to a 100 mL volumetric flask. Add 30 mL of anhydrous formic acid R and sonicate for about 20 minutes. Dilute to volume with solvent mixture, mix and filter. Dilute 5.0 mL of the filtrate to 100.0 mL with the solvent mixture. For solution (2) transfer 25.0 mg of mebendazole RS to a 25 mL volumetric flask, add 10 mL of the

anhydrous formic acid R and sonicate to dissolve. Dilute to volume with the solvent mixture. Dilute 5.0 mL of this solution to 100.0 mL with the solvent mixture.

Operate with a flow rate of 1.2 mL per minute. As a detector use an ultraviolet spectrophotometer set at a wavelength of 250 nm.

Inject alternately 10 µL each of solutions (1) and (2).

Measure the areas of the peaks corresponding to mebendazole obtained in the chromatograms from solution (1) and (2) and calculate the percentage content of mebendazole ($C_{16}H_{13}N_3O_3$) in the chewable tablets using the declared content of $C_{16}H_{13}N_3O_3$ in mebendazole RS.

Impurities

The impurities limited by the requirements of this monograph includes impurity A listed in the monograph for Mebendazole.