Edition: BP 2025 (Ph. Eur. 11.6 update)

Mebendazole Chewable Tablets

General Notices

Action and use

Benzimidazole antihelminthic.

DEFINITION

Mebendazole Chewable Tablets contain Mebendazole.

The tablets comply with the requirements stated under Tablets and with the following requirements.

PRODUCTION

The formulation and production of Mebendazole chewable tablets are designed to control and minimise 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 the mebendazole in the tablets is predominantly in the form of polymorph C. The acceptable crystalline form corresponds to *mebendazole EPCRS*.

Content of mebendazole, $C_{16}H_{13}N_3O_3$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of the powdered tablets containing 50 mg of Mebendazole with 20 mL of *water*. Filter, retain the residue and wash with three 10-mL quantities of *water* and dry overnight under vacuum at room temperature. The *infrared absorption spectrum* of the residue, Appendix II A at 3405 cm^{-1} and 1720 cm^{-1} is concordant with the Mebendazole polymorph C (*RS 503*). The presence of different polymorphic forms is indicated by differences in the spectra at 3405 cm^{-1} and 1720 cm^{-1}.

TESTS

Dissolution

Comply with the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 75 revolutions per minute.
(b) Use 900 mL of 0.1M *hydrochloric acid*, containing 1.0% w/v *sodium lauryl sulfate*, at a temperature of 37°, as the medium.

PROCEDURE

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) After 120 minutes withdraw a sample of the medium and filter. Use the filtered medium, diluted with dissolution medium, if necessary, to produce a solution expected to contain 0.011% w/v of Mebendazole.
(2) 0.011% w/v of *mebendazole BPCRS* in the dissolution medium.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.6 mm) packed with *base-deactivated octadecylsilyl silica gel for chromatography* (3 µm) (Hypersil BDS is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.2 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 250 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

25 volumes of *acetonitrile* and 75 volumes of a 0.75% w/v of *ammonium acetate*.

DETERMINATION OF CONTENT

Calculate the total content 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 BPCRS*.

LIMITS

The amount of Mebendazole released is not less than 75% (Q) of the stated amount.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Mix with the aid of ultrasound a quantity of the powdered tablets containing 0.1 g of Mebendazole in 30 mL of *anhydrous formic acid*. Dilute with *methanol (60%)* to produce 100 mL, mix, and filter.
(2) Dilute 1 volume of solution (1) to 100 volumes with *methanol (60%)*. Dilute 1 volume of the resulting solution to 4 volumes with *methanol (60%)*.
(3) To 10 mg of *mebendazole BPCRS* add 5 mL of *methanol* and 1 mL of 1M *sodium hydroxide*. Heat in a water bath at 60 ° for 1 hour, cool to room temperature, and adjust to pH 7 with 1M *hydrochloric acid*. Dilute to 10 mL with *methanol* and mix (generation of impurity A).
(4) 0.1% w/v of *mebendazole for system suitability EPCRS* in *dimethylformamide*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.6 mm) packed with *base-deactivated octadecylsilyl silica gel for chromatography* (3 µm) (Hypersil BDS is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1.2 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 250 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

Mobile phase A 0.75% w/v of *ammonium acetate* in *water*.

Mobile phase B *acetonitrile*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-15	80→70	20→30	isocratic
15-20	70→10	30→90	linear gradient

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
20-25	10	90	isocratic
25-26	10→80	90→20	linear gradient
26-36	80	20	re-equilibration

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to mebendazole (retention time, about 12 min) are: impurity A, about 0.4; impurity B, about 0.5; impurity C, about 0.7; impurity D, about 1.1; impurity E, about 1.3; impurity F, about 1.4; impurity G, about 1.6.

SYSTEM SUITABILITY

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

LIMITS

Identify any peak in solution (1) corresponding to impurity G using the chromatogram obtained with solution (4) and multiply the area of this peak by a correction factor of 1.4.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity G is not greater than 2 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.25%);

the sum of the areas of all *secondary peaks* is not greater than 4 times the area of the principal peak in the chromatogram obtained with solution (2) (1%).

Disregard any peak with an area less than 0.4 times the area of the principal peak in the chromatogram obtained with solution (2) (0.1%).

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Mix with the aid of ultrasound a quantity of the powdered tablets containing 0.1 g of Mebendazole in 30 mL of *anhydrous formic acid*. Dilute with *methanol (60%)* to produce 100 mL, mix, and filter. Dilute 1 volume of the filtrate to 20 volumes with *methanol (60%)* .
(2) Dissolve with the aid of ultrasound 25 mg of *mebendazole BPCRS* in 10 mL of *anhydrous formic acid*. Dilute with *methanol (60%)* to produce 25 mL. Dilute 1 volume of the solution to 20 volumes with *methanol (60%)*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used.

DETERMINATION OF CONTENT

Calculate the content of mebendazole, $C_{16}H_{13}N_3O_3$, in the tablets, using the declared content of $C_{16}H_{13}N_3O_3$, in *mebendazole BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Mebendazole.