Albendazole chewable tablets (Albendazoli compressi manducabili)

2025-01

Category. Anthelminthic.

Storage. Albendazole tablets should be kept in a tightly closed container, protected from light.

Labelling. The designation on the container should state that the tablets may be chewed, swallowed whole or crushed and mixed with food or liquid and that the tablets should be crushed before being given to a young child.

Additional information. Strengths in the current WHO Model List of Essential Medicines (EML): 400 mg and 200 mg. Strengths in the current EML for children: 400 and 200 mg.

Requirements

Comply with the monograph for *Tablets*.

Definition. Albendazole chewable tablets contain Albendazole in a suitable base that may contain flavouring agents. They contain not less than 90.0% and not more than 110.0% of the amount of Albendazole ($C_{12}H_{15}N_3O_2S$) stated on the label.

Identity tests

Any two of tests A, B or C may be applied:

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 6 volumes of dichloromethane R, 1 volume of ethyl acetate R and 1 volume of glacial acetic acid R as the mobile phase. Apply separately to the plate 10 µL each of the following solutions in a mixture of 9 volumes of dichloromethane R and 1 volume of glacial acetic acid R. For solution (A), shake a quantity of the powdered tablets, nominally containing about 50 mg of Albendazole, with 50 mL, filter and use the filtrate. For solution (B), use a solution containing 1 mg of albendazole RS per mL. After removing the plate from the chromatographic chamber, allow the plate to dry in a current of warm air and examine the chromatogram under ultraviolet light (254 nm).

The principal spot obtained with solution (A) corresponds in position, appearance and intensity with the spot due to albendazole obtained with solution (B).

Carry out the test as described under *1.14.1 Chromatography*, High-performance liquid chromatography, using the conditions given under "Assay", Method A. The retention time of the principal peak in the chromatogram obtained with solution (1) corresponds to the retention time of the peak due to albendazole in the chromatogram obtained with solution (2).

Carry out the test described under "Assay", Method B. The absorption spectrum (*1.6*) of the test solution, when observed between 220 and 340 nm, exhibits maxima at about 231 nm and at about 308 nm.

Alternatively, and in combination with identity test B, where a diode array detector is available, record the UV spectra of the principal peaks in the chromatograms with a diode array detector in the range of 220 nm to 400 nm. The UV spectrum of the principal peak in the chromatogram obtained with solution (1) corresponds to the UV spectrum of the peak due to albendazole in the chromatogram obtained with solution (2).

Dissolution. *For 200 mg tablets*: carry out the test as described under *5.5 Dissolution test for oral dosage forms* using 900 mL of hydrochloric acid (~3.65 g/L)TS as the dissolution medium and rotating the paddle at 50 revolutions per minute. At 30 minutes, withdraw a sample of about 10 mL of the dissolution medium through an in-line filter. Cool the filtered sample to room temperature and dilute 2.0 mL of the obtained solution to 25.0 mL with the dissolution medium.

Measure the absorbance (*1.6*) of a 1.0 cm layer of the solution at about 291 nm, using hydrochloric acid (~3.65 g/L) TS as the blank. For each of the tablets tested, calculate the total amount of albendazole ($C_{12}H_{15}N_3O_2S$) in the medium using the absorptivity value of 37.6 ($A^{1\%}_{1\ cm}$ = 376). The amount of albendazole released is not less than 80% (Q) of the amount declared on the label.

For 400 mg tablets: carry out the test as described under *5.5 Dissolution test for oral dosage forms* using 900 mL of hydrochloric acid (~10 g/L) TS as the dissolution medium and rotating the paddle at 50 revolutions per minute. At 30 minutes, withdraw a sample of about 10 mL of the dissolution medium through an in-line filter. Cool the filtered sample to room temperature and dilute 2.0 mL of the obtained solution to 50.0 mL with the dissolution medium.

Measure the absorbance (*1.6*) of a 1.0 cm layer of the solution at about 291 nm, using hydrochloric acid (~10 g/L) TS as the blank. For each of the tablets tested, calculate the total amount of albendazole ($C_{12}H_{15}N_3O_2S$) in the medium using the

absorptivity value of 37.6 ($A^{1\%}_{1\ cm}$ = 376). The amount of albendazole released is not less than 80% (Q) of the amount declared on the label.

Related substances. Prepare the solutions immediately before use. Carry out the test as described under *1.14.1 Chromatography , High-performance liquid chromatography*, using a stainless steel column (15 cm × 3.9 mm) packed with particles of silica gel, the surface of which has been modified with chemically-bonded octadecylsilyl groups (4 µm).

Use the following conditions for gradient elution:

mobile phase A: a solution of 1.15 g of ammonium dihydrogen phosphate R in 1000 mL of water R; and

mobile phase B: methanol R.

Time (minutes)	Mobile phase A (% *V*/*V*)	Mobile phase B (% *V*/*V*)	Comments
0–3	70 to 66	30 to 34	Linear gradient
3–13	66 to 50	34 to 50	Linear gradient
13–43	50	50	Isocratic
43–45	50 to 70	50 to 30	Return to initial composition
45–55	70	30	Re-equilibration

Operate with a flow rate of 0.8 mL per minute. As a detector, use an ultraviolet spectrophotometer set at a wavelength of 254 nm.

Prepare the following solutions. For solution (1), transfer a quantity of the powdered tablets, nominally containing 200.0 mg of Albendazole, to a 100 mL volumetric flask. Add 10 mL of sulfuric acid/methanol (1%) TS and 25 mL of methanol R and sonicate for 15 minutes. Shake for a further 15 minutes. Dilute to volume with methanol R, mix and allow the insoluble to settle. Dilute 5.0 mL of the supernatant liquid to 50.0 mL with methanol R and filter the solution. For solution (2), dilute 1.0 mL of solution (1) to 100.0 mL with methanol R. For solution (3), dilute 1.0 mL of solution (2) to 10.0 mL with methanol R. For solution (4), dissolve about 5 mg of albendazole for system suitability RS (containing albendazole and the impurities B, C, E, F and H) in 1 mL of sulfuric acid/methanol (1%) TS and dilute to 10 mL with the mobile phase. For solution (5), dilute 1 mL of sulfuric acid/methanol (1%) TS to 10 mL with mobile phase. Use 1 mL of this solution to dissolve the content of a vial of albendazole impurity mixture RS (containing the impurities A and D).

Inject alternately 20 µL each of solutions (1), (2), (3), (4) and (5).

Use the chromatogram obtained with solution (4) to identify the peaks due to the impurities B, C, E, F and H. Use the chromatogram obtained with solution (5) to identify the peaks due to the impurities A and D. The impurities are eluted at the following relative retention with reference to albendazole (retention time 32 minutes): impurity D about 0.13, impurity E about 0.25, impurity B and impurity C about 0.28, impurity F about 0.48, impurity A about 0.56 and impurity H about 0.69.

The test is not valid unless, in the chromatogram obtained with solution (4), the resolution factor between the peak due to impurity E and the peak due to impurities B and C (impurities B and C co-elute) is at least 1.5. Also, the test is not valid unless, in the chromatogram obtained with solution (3), the peak due to albendazole is detected with a signal-to-noise ratio of at least 20.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to either impurity A, when multiplied by a correction factor of 1.4, is not greater than the area of the peak due to albendazole in the chromatogram obtained with solution (2) (1.0%);

the sum of the areas of any peaks corresponding to impurities B and C (impurities B and C co-elute), when multiplied by a correction factor of 1.4, is not greater than the area of the peak due to albendazole in the chromatogram obtained with solution (2) (1.0%);

the area of any peak corresponding to either impurity D, when multiplied by a correction factor of 1.9, is not greater than the area of the peak due to albendazole in the chromatogram obtained with solution (2) (1.0%);

the area of any peak corresponding to impurity E, when multiplied by a correction factor of 1.4, is not greater than 0.3 times the area of the peak due to albendazole in the chromatogram obtained with solution (2) (0.3%);

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

the area of any peak corresponding to impurity H is not greater than 0.6 times the area of the peak due to albendazole in the chromatogram obtained with solution (2) (0.6%);

the area of any other impurity peak is not greater than twice the area of the peak due to albendazole in the chromatogram obtained with solution (3) (0.2%).

The sum of the area of all impurity peaks, including the corrected areas of any peaks corresponding to impurities A, B/C, D and E is not greater than three times the area of the peak due to albendazole in the chromatogram obtained with solution (2) (3.0%). Disregard any peak with an area less than the area of the peak due to albendazole in the chromatogram obtained with solution (3) (0.1%).

Assay

Either method A or method B may be applied.

Carry out the test as described under *1.14.1 Chromatography*, High-performance liquid chromatography, using a stainless steel column (15 cm × 3.9 mm) packed with particles of silica gel, the surface of which has been modified with chemically-bonded octadecylsilyl groups (4 µm).

As the mobile phase, use a solution prepared as follows: dissolve 1.15 g of ammonium dihydrogen phosphate R in 1000 mL of water R. Mix 400 mL of this solution with 600 mL of methanol R.

For solution (1), weigh and powder 20 tablets. Transfer a quantity of the powdered tablets, nominally containing 100.0 mg of Albendazole, to a 50 mL volumetric flask. Add 10 mL of sulfuric acid/methanol (1%) TS and 25 mL of methanol R and sonicate for 15 minutes. Shake for further 15 minutes. Dilute to volume with methanol R, mix and allow the insoluble to settle. Dilute 5.0 mL of the supernatant liquid to 50.0 mL with mobile phase and filter the solution. For solution (2), transfer 50.0 mg of albendazole RS to a 250 mL volumetric flask, add 10 mL of sulfuric acid/methanol (1%) TS and 25 mL of methanol R and sonicate for 15 minutes. Dilute to volume with mobile phase and mix.

Operate with a flow rate of 0.8 mL per minute. As a detector, use an ultraviolet spectrophotometer set at a wavelength of 254 nm.

Inject 20 µL each of solutions (1) and (2). Record the chromatograms for about 1.5 times the retention time of albendazole.

Measure the areas of the peaks corresponding to albendazole obtained in the chromatograms from solutions (1) and (2) and calculate the percentage content of Albendazole ($C_{12}H_{15}N_3O_2S$) in the tablets using the declared content of $C_{12}H_{15}N_3O_2S$ in albendazole RS.

Weigh and powder 20 tablets. Transfer a quantity of the powdered tablets, nominally containing about 20.0 mg of Albendazole, to a 50 mL volumetric flask, add 30 mL of hydrochloric acid/methanol (0.01 mol/L) VS, shake for 15 minutes and dilute to volume with the same solvent. Mix and filter, discarding the first 10 mL of the filtrate. Dilute 2.0 mL of the filtrate to 100.0 mL with sodium hydroxide (0.1 mol/L) VS. Measure the absorbance of the resulting solution at the maximum at about 308 nm, using sodium hydroxide (0.1 mol/L) VS as the blank. Calculate the content of Albendazole ($C_{12}H_{15}N_3O_2S$), using the absorptivity value of 74.2 ($A^{1\%}_{1\ cm}$ = 742)

Impurities. The impurities limited by the requirements of this monograph include those listed in the monograph on Albendazole.