ALBENDAZOLE CHEWABLE TABLETS
Revised draft proposal for *The International Pharmacopoeia* (July 2013)

DRAFT FOR COMMENTS

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### SCHEDULE FOR THE ADOPTION PROCESS OF DOCUMENT QAS/11.455

**Draft proposal for the International Pharmacopoeia**

**CHEWABLE ALBENDAZOLE TABLETS**

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ALBENDAZOLE CHEWABLE TABLETS
Revised draft proposal for The International Pharmacopoeia

**Category.** Anthelminthic.

**Storage.** Albendazole 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 or crushed and mixed with food or liquid, and the tablets should be crushed before giving to a young child.

**Additional information.** Strengths in the current WHO Model list of essential medicines: 400 mg. Strengths in the current WHO Model list of essential medicines for children: 400 mg.

**Requirements**

Comply with the monograph for Tablets.

**Definition.** Albendazole chewable tablets contain Albendazole in a suitable basis that may contain suitable flavoring agents. They contain not less than 90.0% and not more than 110.0% of the amount of Albendazole \((C_{12}H_{15}N_{3}O_{2}S)\) stated on the label.

**Identity tests**

- Either tests A, C and D or tests B, C and D may be applied

A. Carry out the test as described under 1.14.1 Thin-layer chromatography, using silica gel R5 as the coating substance and a mixture of dichloromethane R, glacial acetic acid R, and ether R \((30:7:3 \text{ v/v})\) 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 containing about 2.5 mg of Albendazole with 25 ml, filter and use the filtrate. For solution (B) use 0.1 mg of albendazole RS per ml. For solution (C) use 0.1 mg of albendazole RS and 0.1 mg of oxibendazole R 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 \((254 \text{ nm})\). The test is not valid unless the chromatogram obtained with solution (C) shows two clearly separated spots.

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

B. See the test described below under Assay, Method A. The retention time of the principal peak in the chromatogram obtained with solution (1) is similar to the retention time of the peak due to albendazole obtained with solution (3).

C. See 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 308 nm. The absorbance of a 1 cm layer at 308 nm is about 0.59.

D. Suspend a quantity of powdered tablets containing about 0.2 g of Albendazole in 30 ml of ethanol R by warming in a water-bath. Filter and evaporate the filtrate to dryness. Ignite about 0.1 g of the residue; fumes are evolved, staining lead acetate paper R black.

Disintegration. Comply with 5.3 Disintegration test for tablets and capsules. Operate the apparatus for 15 minutes and examine the state of the tablets.

Related substances

A. Carry out the test as described under 1.14.4 High performance liquid chromatography, using the conditions given below under Assay, method A.

Prepare the following solutions.

Solvent mixture: dilute 1 volume of sulfuric acid R with 99 volumes of methanol R.

For solution (1) transfer a quantity of the powdered tablets containing about 25 mg of Albendazole to a 50 ml volumetric flask. Add 5 ml of the solvent mixture and 20 ml of methanol R and shake to dissolve for about 15 minutes. Dilute to volume with methanol R. For solution (2) dilute 1.0 ml of solution (1) to 100.0 ml with methanol R. For solution (3) dissolve about 20 mg of albendazole RS and about 20 mg of oxibendazole R in 5 ml of solvent mixture and dilute to 100.0 ml with methanol R.

Inject separately 20 µl each of solutions (1), (2) and (3). Record the chromatogram for about 25 minutes.

In the chromatogram obtained with solution (3) the peak due to oxibendazole is eluted at a retention time about 9.9 min and the peak due to albendazole at a retention time about 13.6 minutes. The test is not valid unless the resolution factor between the peak due to oxibendazole and the peak due to albendazole is at least 3.0.

In the chromatogram obtained with solution (1) the area of any peak, other than the principal peak, is not greater than 0.75 times the area of the peak due to albendazole in the chromatogram obtained with solution (2) (0.75%).
B. Carry out the test as described under *1.14.1 Thin-layer chromatography*, using silica gel R5 as the coating substance and a mixture of dichloromethane R, glacial acetic acid R, and ether R (30:7:3 v/v) 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 containing about 250 mg of Albendazole with 25 ml, filter and use the filtrate. For solution (B) use 0.1 mg of albendazole RS per ml. For solution (C) use 0.05 mg of albendazole RS per ml. For solution (D) use 0.1 mg albendazole RS and 0.1 mg oxibendazole R per ml. After removing the plate from the chromatographic chamber, allow the plate to dry in a current of warm air. Examine the chromatogram in ultraviolet light (254 nm). The test is not valid unless the chromatogram obtained with solution (D) shows two clearly separated spots.

In the chromatogram obtained with solution (A) any spot, other than the principal spot, is not more intense than the principal spot obtained with solution B (1.0%) and not more than one spot is more intense than the principal spot obtained with solution (C) (0.5%).

**Assay**

- Either method A or method B may be applied.

A. Carry out the test as described under *1.14.4 High-performance liquid chromatography*, using a stainless steel column (25 cm × 4.6 mm) packed with octadecylsilyl base-deactivated silica gel for chromatography R (5 µm).\(^1\)

As the mobile phase, use a solution prepared as follows: dissolve 1.67 g of monobasic ammonium phosphate R in 1000 ml of water R, mix and filter. Mix 300 ml of this solution with 700 ml of methanol R. Make adjustments if necessary.

Prepare the following solutions.

Solvent mixture: dilute 1 volume of sulfuric acid R with 99 volumes of methanol R.

For solution (1) weigh and powder 20 tablets. Transfer a quantity of the powdered tablets, containing about 100 mg of Albendazole, accurately weighed, to a 50 ml volumetric flask. Add 5 ml of the solvent mixture and 20 ml of methanol R and shake for about 15 minutes. Dilute to volume with methanol R, mix and filter, discarding the first 15 ml of the filtrate. Dilute 5.0 ml of this solution to 50.0 ml with methanol R. For solution (2) transfer

\(^1\) Inertsil ODS-SP has been found suitable.
25.0 mg of Albendazole RS to a 25 ml volumetric flask, add 5 ml of the solvent mixture and 15 ml of methanol R and shake to dissolve. Dilute to volume with methanol R. For solution (3) dilute 2.0 ml of solution (2) to 10.0 ml with methanol R. For solution (4) dissolve about 20 mg of oxibendazole R in 5 ml of solvent mixture in a 100 ml volumetric flask, add 20 ml of solution (2), mix and dilute to volume with methanol R.

Operate with a flow rate of 0.7 ml per minute. As a detector use an ultraviolet spectrophotometer set at a wavelength of 254 nm.

Inject separately 20 µl each of solutions (1), (3) and (4). The test is not valid unless in the chromatogram obtained with solution (4) the resolution factor between the peaks due to albendazole and due to oxibendazole is at least 3.0.

Measure the areas of the peak responses obtained in the chromatograms from solutions (1) and (3) and calculate the content of Albendazole (C₁₂H₁₅N₃O₂S) in the tablets, using the declared content of C₁₂H₁₅N₃O₂S in albendazole RS.

B. Weigh and powder 20 tablets. Transfer a quantity of the powdered tablets containing about 20 mg of Albendazole, accurately weighed, 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. Transfer 1.0 ml of the subsequent filtrate to a 50 ml volumetric flask and dilute to volume with sodium hydroxide (~4 g/l) TS. Measure the absorbance of the resulting solution at the maximum at about 308 nm. Calculate the content of Albendazole (C₁₂H₁₅N₃O₂S), using the absorptivity value of 74.2 (A₁cm⁻¹ = 742).

Reagents to be added to The International Pharmacopoeia

Oxibendazole R

Oxibendazole of a suitable quality should be used.

Sodium hydroxide (~4 g/l) TS

A solution of sodium hydroxide R containing about 4 g/l of NAOH (approximately 0.1 mol/l)