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ALBENDAZOLE CHEWABLE TABLETS
(ALBENDAZOLI COMPRESSI MANDUCABILI)

Draft proposal for revision for *The International Pharmacopoeia*
(November 2020)

DRAFT FOR COMMENTS

Please send any comments you may have on this draft working document to **Dr Herbert Schmidt**, Technical Officer, Norms and Standards for Pharmaceuticals, Technical Standards and Specifications (schmidth@who.int), with a copy to Claire Vogel (vogelc@who.int) by **15 January 2021**.

Working documents are sent out electronically and they will also be placed on the WHO Medicines website (http://www.who.int/medicines/areas/quality_safety/quality_assurance/guidelines/en/) for comments under the “Current projects” link. If you wish to receive our draft guidelines, please send your e-mail address to jonessi@who.int and your name will be added to our electronic mailing list.

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38 SCHEDULE FOR THE ADOPTION PROCESS OF DOCUMENT QAS/20.855/Rev.1:

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ALBENDAZOLE CHEWABLE TABLETS
(ALBENDAZOLI COMPRESSI MANDUCABILI)

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Description	Date
Meeting of the Working Group on Albendazole of <i>The International Pharmacopoeia</i> .	July 2020
Drafting of the revision based on information received by a manufacturer.	July 2020
Draft revision sent out for public consultation.	August-September 2020
Presentation to the Fifty-fifth WHO Expert Committee on Specifications for Pharmaceutical Preparations.	October 2020
Drafting of revision 1 based on the comments received during the first public consultation and made at the Fifty-fifth WHO Expert Committee on Specifications for Pharmaceutical Preparations	November 2020
Revision 1 sent out for public consultation.	November 2020 – January 2021
Further follow-up action as required.	

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44 *[Note from the Secretariat. It is proposed to revise the Dissolution test in monograph on*
45 *Albendazole chewable tablets based on information received by a manufacturer. Comments*
46 *are invited on the revised section.*

47 *Changes from the current monograph are indicated in the text by insert or ~~delete~~.]*

48

49 **ALBENDAZOLE CHEWABLE TABLETS**
50 **(ALBENDAZOLI COMPRESSI MANDUCABILI)**

51 **Category.** Anthelmintic.

52 **Storage.** Albendazole chewable tablets should be kept in a tightly closed container.

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

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

58 **Requirements**

59 Comply with the monograph for [Tablets](#).

60 **Definition.** Albendazole chewable tablets contain Albendazole in a suitable basis that may
61 contain suitable flavouring agents. They contain not less than 90.0% and not more than 110.0%
62 of the amount of Albendazole (C₁₂H₁₅N₃O₂S) stated on the label.

63 **Identity tests**

64 • Any two of tests A, B and C may be applied.

65 A. Carry out the test as described under [1.14.1 Thin-layer chromatography](#) using the
66 chromatographic conditions given under “Related substances”, Test B. Apply
67 separately to the plate 10 µL each of the following solutions in a mixture of 9 volumes
68 of dichloromethane R and 1 volume of glacial acetic acid R. For solution (A), shake a
69 quantity of the powdered tablets containing about 2.5 mg of Albendazole with 25 mL,
70 filter and use the filtrate. For solution (B), use 0.1 mg of albendazole RS per mL. For
71 solution (C), use 0.1 mg of albendazole RS and 0.1 mg of oxibendazole R per mL.
72 After removing the plate from the chromatographic chamber, allow the plate to dry in
73 a current of warm air and examine the chromatogram under ultraviolet light (254 nm).

74 The test is not valid unless the chromatogram obtained with solution (C) shows two
75 clearly separated spots.

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

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

81 C. See the test described under “Assay”, Method B. The [absorption spectrum \(1.6\)](#) of the
82 test solution, when observed between 220 and 340 nm, exhibits maxima at about 231
83 nm and at 308 nm; the absorbance at 308 nm is about 0.59.

84 **Dissolution**

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

91 Measure the absorbance (1.6) of a 1.0 cm layer of the solution at about 291 nm, using
92 hydrochloric acid (~3.65 g/L) TS as the blank. For each of the six tablets tested, calculate the
93 total amount of albendazole (C₁₂H₁₅N₃O₂S) in the medium using the absorptivity value of 37.6
94 (A_{1 cm}^{1%} = 376). The amount of albendazole released is not less than 80% (Q) of the amount
95 declared on the label.

96 For 400 mg tablets: carry out the test as described under 5.5 Dissolution test for solid oral
97 dosage forms using 900 mL of hydrochloric acid (~10 g/L) TS as the dissolution medium and
98 rotating the paddle at 50 revolutions per minute. At 30 minutes, withdraw a sample of about
99 10 mL of the dissolution medium through an in-line filter. Cool the filtered sample to room
100 temperature and dilute 2.0 mL of the obtained solution to 50.0 mL with the dissolution medium.

101 Measure the absorbance (I.6) of a 1.0 cm layer of solutions (1) and (2) at about 291 nm, using
102 hydrochloric acid (~10 g/L) TS as the blank. For each of the six tablets tested, calculate the
103 total amount of albendazole (C₁₂H₁₅N₃O₂S) in the medium using the absorptivity value of 37.6
104 (A_{1cm}^{1%} = 376). The amount of albendazole released is not less than 80% (Q) of the amount
105 declared on the label.

106 Carry out the test as described under [5.5 Dissolution test for solid oral dosage forms](#) using 900
107 mL of hydrochloric acid (~3.65 g/L) TS as the dissolution medium and rotating the paddle at
108 75 revolutions per minute. At 30 minutes withdraw a sample of about 15 mL of the dissolution
109 medium through an in-line filter. Cool the filtered sample to room temperature. Transfer 1.0
110 mL of the clear filtrate to a 50 mL volumetric flask and dilute to volume with sodium hydroxide
111 (0.1 mol/L) VS. Measure the absorbance (I.6) of a 1 cm layer of the resulting solution at the
112 maximum at about 308 nm, using sodium hydroxide (0.1 mol/L) VS as the blank.

113 For each of the six tablets tested calculate the total amount of albendazole (C₁₂H₁₅N₃O₂S) in
114 the medium using the absorptivity value of 74.2 (A_{1cm}^{1%} = 742). The amount in solution for each
115 tablet is not less than 80% (Q) of the amount declared on the label.

116 **Related substances**

- 117 • Either method A or method B may be applied.
- 118 A. Carry out the test as described under [1.14.4 High-performance liquid chromatography](#)
119 using the conditions given below under “Assay”, Method A.

120 Prepare the following solutions.

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

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

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

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

134 In the chromatogram obtained with solution (1):

- 135 • the area of any peak, other than the principal peak, is not greater than the area
136 of the peak due to albendazole in the chromatogram obtained with solution (2)
137 (1.0%); and
- 138 • the area of not more than one such peak is greater than 0.75 times the area of
139 the peak due to albendazole in the chromatogram obtained with solution (2)
140 (0.75%).

141 B. Carry out the test as described under [1.14.1 Thin-layer chromatography](#) using silica gel
142 R5 as the coating substance and a mixture of dichloromethane R, glacial acetic acid R
143 and ether R (30:7:3 v/v) as the mobile phase. Apply separately to the plate 10 μ L each
144 of the following solutions in a mixture of 9 volumes of dichloromethane R and 1 volume
145 of glacial acetic acid R. For solution (A), shake a quantity of the powdered tablets
146 containing about 250 mg of Albendazole with 25 mL, filter and use the filtrate. For
147 solution (B), use 0.1 mg of albendazole RS per mL. For solution (C), use 0.075 mg of
148 albendazole RS per mL. For solution (D), use 0.1 mg albendazole RS and 0.1 mg
149 oxibendazole R per mL. After removing the plate from the chromatographic chamber,
150 allow the plate to dry in a current of warm air. Examine the chromatogram in ultraviolet
151 light (254 nm). The test is not valid unless the chromatogram obtained with solution
152 (D) shows two clearly separated spots.

153 In the chromatogram obtained with solution (A), any spot, other than the principal spot,
154 is not more intense than the principal spot obtained with solution (B) (1.0%) and not
155 more than one spot is more intense than the principal spot obtained with solution (C)
156 (0.75%).

157 **Assay**

158 • Either method A or method B may be applied.

159 A. Carry out the test as described under [1.14.4 High-performance liquid chromatography](#)
160 using a stainless steel column (25 cm × 4.6 mm) packed with octadecylsilyl base-
161 deactivated silica gel for chromatography R (5 µm).

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

165 Prepare the following solutions.

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

167 For solution (1), weigh and powder 20 tablets. Transfer a quantity of the powdered
168 tablets containing about 100.0 mg of Albendazole, ~~accurately weighed~~, to a 50 mL
169 volumetric flask. Add 5 mL of the solvent mixture and 20 mL of methanol R and shake
170 for about 15 minutes. Dilute to volume with methanol R, mix and filter, discarding the
171 first 15 mL of the filtrate. Dilute 5.0 mL of this solution to 50.0 mL with methanol R.
172 For solution (2), transfer 25.0 mg of Albendazole RS to a 25 mL volumetric flask, add
173 5 mL of the solvent mixture and 15 mL of methanol R and shake to dissolve. Dilute to
174 volume with methanol R. For solution (3), dilute 2.0 mL of solution (2) to 10.0 mL
175 with methanol R. For solution (4), dissolve about 20 mg of oxibendazole R in 5 mL of
176 solvent mixture in a 100 mL volumetric flask, add 20 mL of solution (2), mix and dilute
177 to volume with methanol R.

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

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

183 Measure the areas of the peak responses obtained in the chromatograms from solutions
184 (1) and (3) and calculate the content of Albendazole ($C_{12}H_{15}N_3O_2S$) in the tablets using
185 the declared content of $C_{12}H_{15}N_3O_2S$ in albendazole RS.

186 B. Weigh and powder 20 tablets. Transfer a quantity of the powdered tablets containing
187 ~~about 20.0 mg of Albendazole, accurately weighed,~~ to a 50 mL volumetric flask, add
188 30 mL of hydrochloric acid/methanol (0.01 mol/L) VS, shake for 15 minutes and dilute
189 to volume with the same solvent. Mix and filter, discarding the first 10 mL of the
190 filtrate. Transfer 1.0 mL of the subsequent filtrate to a 50 mL volumetric flask and
191 dilute to volume with sodium hydroxide (0.1 mol/L) VS. Measure the absorbance of
192 the resulting solution at the maximum at about 308 nm, using sodium hydroxide (0.1
193 mol/L) VS as the blank. Calculate the content of Albendazole ($C_{12}H_{15}N_3O_2S$), using
194 the absorptivity value of 74.2 ($A_{1\text{ cm}}^{1\%} = 742$).

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Draft for comments