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## DAPSONE TABLETS (DAPSONI COMPRESSI)

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3 **Draft proposal for revision in *The International Pharmacopoeia***

4 (16 December 2025)

5 **DRAFT FOR COMMENTS**

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For any technical questions, you may contact **Dr Herbert Schmidt**, Technical Officer, Norms and Standards for Pharmaceuticals, Technical Standards and Specifications ([schmidth@who.int](mailto:schmidth@who.int)), with a copy to **Ms Sinéad Jones** ([jonessi@who.int](mailto:jonessi@who.int), [nsp@who.int](mailto:nsp@who.int)).

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37                   **SCHEDULE FOR DRAFT WORKING DOCUMENT QAS/23.920**

38                   **DAPSONE TABLETS (DAPSONI COMPRESSI)**

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<b>Description</b>	<b>Date</b>
Drafting of the monograph based on information found in the public domain and other pharmacopoeias.	January 2023
Discussion at the Consultation on Quality Control and Pharmacopoeial Specifications.	April 2023
Discussion at the Consultation on Quality Control and Pharmacopoeial Specifications.	May 2024
Discussion at the Consultation on Quality Control and Pharmacopoeial Specifications	April 2025
Discussion at the 59 <sup>th</sup> meeting of the WHO Expert Committee on Specifications for Pharmaceutical Preparations	October 2025
Public consultation	December 2025 – February 2026
Further follow-up action as required.	

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41    *[Note from the Secretariat. It is intended to revise the monograph on Dapsone*  
42    *tablets. The revision is based on information found in the public domain and in other*  
43    *pharmacopoeias and submitted by a manufacturer.*

44    *Changes are indicated by insert or replace.*]

45

46

## DAPSONE TABLETS (DAPSONI COMPRESSI)

47 **Category.** Antileprosy medicine.

48 **Additional information.** Strengths in the current WHO Model list of essential  
49 medicines: 25 mg, 50 mg, 100 mg. Strengths in the current WHO Model list of  
50 essential medicines for children: 25 mg, 50 mg, 100 mg.

51 **The tablets may be coloured.**

### 52 **Requirements**

53 Comply with the monograph for *Tablets*.

54 Dapsone tablets contain not less than 90.0 93.0% and not more than 110.0 107.0% of  
55 the amount of  $C_{12}H_{12}N_2O_2S$  stated on the label.

### 56 **Identity tests**

57 • Either test A, or any two of tests B, C and D, may be applied. Either tests A and  
58 B or tests B and C may be applied.

59 A. Carry out the test as described under 1.7 Spectrophotometry in the infrared  
60 region. Transfer a quantity of finely powdered Tablets, equivalent to 100 mg of  
61 dapsone, to a suitable container, add 5 mL of acetone R, sonicate for 5 min,  
62 filter, and evaporate the filtrate to dryness. Dry this residue at 105 °C for 1 h.  
63 The infrared absorption spectrum is concordant with the spectrum obtained  
64 from dapsone RS or with the reference spectrum of dapsone.

65 B. To a quantity of the powdered tablets, nominally containing 0.1 g of Dapsone,  
66 add 50 mL of methanol R, shake and filter. Dilute 0.5 mL of the filtrate to 200  
67 mL with methanol R. The absorption spectrum of the resulting solution, when  
68 observed between 230 nm and 350 nm, exhibits maxima at about 260 nm and

69        295 nm; the absorbances of a 1 cm layer at these maximum wavelengths are  
70        about 0.36 and 0.6, respectively.

71        Alternatively, in combination with identity test B, where a diode array detector  
72        is available, record the UV spectra of the principal peaks in the chromatograms  
73        with a diode array detector in the range of 230 nm to 350 nm. The UV  
74        spectrum of the principal peak in the chromatogram obtained with solution (1)  
75        corresponds to the UV spectrum of the peak due to dapsoner in the  
76        chromatogram obtained with solution (2).

77        C. Carry out the test as described under 1.14.1, Chromatography, High-  
78        performance liquid chromatography using the conditions and solutions given  
79        under Assay. The retention time of the principal peak obtained with solution  
80        (1) corresponds to the retention time of the peak due to dapsoner in the  
81        chromatogram obtained with solution (3)

82        D. Carry out the test as described under 1.14.1 Chromatography, Thin-layer  
83        chromatography, using silica gel R6 as the coating substance and a freshly  
84        prepared mixture of dichloromethane R, methanol R and ammonia (~260 g/L)  
85        TS (90:10:2 V/V/V) as the mobile phase. Apply separately to the plate 5 µL of  
86        each of the following 2 solutions: for solution (A), dissolve a quantity of the  
87        powdered tablets, nominally containing 10 mg of dapsoner in 10 mL of  
88        methanol R, centrifuge for 10 minutes and use the supernatant liquid. For  
89        solution (B), use a solution containing 1 mg of dapsoner RS per mL of methanol  
90        R. Develop the plate. After removing the plate from the chromatographic  
91        chamber, allow it to dry in air or in a current of air. Examine the chromatogram  
92        under ultraviolet light (254 nm and 365 nm). The principal spot in the  
93        chromatogram obtained with solution (A) corresponds in position, appearance  
94        and intensity with the spot due to dapsoner in the chromatogram obtained with  
95        solution (B).

96 B. See the test described below under "Related substances". The principal spot  
97 obtained with solution A corresponds in position, appearance and intensity with  
98 that obtained with solution B.

99 C. Shake a quantity of the powdered tablets equivalent to 0.05 g of Dapsone with  
100 5 mL of warm acetone R, filter, evaporate the filtrate and dry at 105 °C for 30  
101 minutes. Dissolve the residue in 2 mL of hydrochloric acid (~70 g/l) TS, cool  
102 in ice and add 4 mL of sodium nitrite (10 g/l) TS. Allow to stand for 2 minutes  
103 then pour the mixture into 2 mL of freshly prepared 2-naphthol TS1 containing  
104 1 g of sodium acetate R; an orange red precipitate is produced.

105 **Related substances.** Carry out the test as described under 1.14.1 Chromatography,  
106 High-performance liquid chromatography, using a stainless steel column (25 cm x 4.6  
107 mm) packed with end-capped particles of silica gel, the surface of which has been  
108 modified with chemically-bonded octadecylsilyl groups (5 µm)<sup>1</sup>.

109 Use the following conditions for gradient elution:

110 • Mobile phase A: water R.  
111 • Mobile phase B: acetonitrile R.

<u>Time</u> <u>(Minutes)</u>	<u>Mobile phase A</u> <u>(% v/v)</u>	<u>Mobile phase B</u> <u>(% v/v)</u>	<u>Comments</u>
0 - 2	80	20	isocratic
2 - 17	80 to 75	20 to 25	linear gradient
17 - 40	75 to 20	25 to 80	linear gradient
40 - 41	20 to 80	80 to 20	return to initial composition
41 - 50	80	20	re-equilibration

112 Operate with a flow rate of 1.0 mL per minute. As a detector, use an ultraviolet  
113 spectrophotometer set at a wavelength of 254 nm.

<sup>1</sup> An Thermo BDS Hypersil C18Column was found suitable.

114 Prepare the following solutions using as the diluent a mixture of 50 volumes of water  
115 R and 50 volumes of acetonitrile R. For solution (1), transfer a quantity of the  
116 powdered tablets, nominally containing 100 mg of dapsone into a 100 mL volumetric  
117 flask, add 70 mL of methanol R, sonicate for 15 minutes at 35 °C with intermittent  
118 shaking, allow to cool to room temperature and add methanol R to volume. Dilute 5.0  
119 mL of the supernatant to 25.0 mL with diluent and filter. For solution (2), dilute 1.0  
120 mL of the solution (1) to 100.0 mL with diluent. For solution (3), dilute 2.0 mL to  
121 20.0 mL. For solution (4), dissolve 2 mg of the test substance, 2 mg of 4-(4-  
122 aminobenzene-1-sulfonyl)phenol R (impurity A), 2 mg of 4-(benzenesulfonyl)aniline  
123 R (impurity B) and 2 mg of 4,4'-[oxybis[(4,1-phenylene)sulfonyl]]dianiline R  
124 (impurity C) and dilute to 50 mL. Dilute 1 mL of this solution to 10 mL.

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

126 Use the chromatogram obtained with solution (4) to identify the peaks due to the  
127 impurities A, B and C. The impurities, if present, are eluted at the following relative  
128 retentions with reference to dapsone (retention time about 10 minutes): impurity I  
129 about 0.15; impurity A about 1.2; impurity G about 1.45; impurity D about 2.2;  
130 impurity B about 2.4; impurity E about 3.0; impurity C about 3.2; impurity F about  
131 3.45; and impurity H about 3.8.

132 The test is not valid unless, in the chromatogram obtained with solution (4), the  
133 resolution between the peaks due to dapsone and impurity A is at least 5.0. Also, the  
134 test is not valid unless, in the chromatogram obtained with solution (3), the peak due  
135 to dapsone is detected with a signal-to-noise ratio of at least 10.

136 In the chromatogram obtained with solution (1):

137 • the area of any peak corresponding to impurity B, when multiplied by a  
138 correction factor of 2.7, is not greater than 0.4 times the area of the peak due to  
139 dapsone in the chromatogram obtained with solution (2) (0.4 %);

140 • the area of any peak corresponding to impurity A, when multiplied by a  
141 correction factor of 1.9, is not greater than 0.3 times the area of the peak due to  
142 dapsone in the chromatogram obtained with solution (2) (0.3 %);  
143 • the area of any peak corresponding to impurity C, when multiplied by a  
144 correction factor of 1.7, is not greater than 0.3 times the area of the peak due to  
145 dapsone in the chromatogram obtained with solution (2) (0.3 %);  
146 • the area of any other impurity peak is not greater than 0.2 times the area of the  
147 peak due to dapsone in the chromatogram obtained with solution (2) (0.2 %).  
148 • The sum of the areas of all impurity peaks, including the corrected areas of any  
149 peaks corresponding to impurities A, B and C is not greater than 1.5 times the  
150 area of the peak due to dapsone in the chromatogram obtained with solution (2)  
151 (1.5%). Disregard any peak with an area less than the area of the peak due to  
152 dapsone in the chromatogram in the chromatogram obtained with solution (3)  
153 (0.1%).

154 Carry out the test as described under 1.14.1 Chromatography, Thin layer  
155 chromatography using silica gel R1 as the coating substance and a mixture of 8  
156 volumes of toluene R and 4 volumes of acetone R as the mobile phase. Apply  
157 separately to the plate 1 µl of each of the following two solutions. For solution (A)  
158 shake a quantity of the powdered tablets equivalent to 10 mg of Dapsone with 10 mL  
159 of methanol R, filter and use the clear filtrate. For solution (B) dissolve 5 mg of  
160 dapsone RS in 5 mL of methanol R. Further apply 10 µl of the following three  
161 solutions. For solution (C) shake a quantity of the powdered tablets equivalent to 0.1 g  
162 of Dapsone with 10 mL of methanol R, filter and use the clear filtrate. For solution  
163 (D) dilute 1 mL of solution C to 100 mL with methanol R and for solution (E) dilute 1  
164 mL of solution D to 5 mL with methanol R. After removing the plate from the  
165 chromatographic chamber allow it to dry in air and spray first with sodium  
166 nitrite/hydrochloric acid TS and then, while still damp, with N (1  
167 naphthyl)ethylenediamine hydrochloride (1 g/l) TS, and examine the chromatogram in  
168 daylight.

169 ~~Any spot obtained with solution C, other than the principal spot, is not more intense~~  
170 ~~than that obtained with solution D and not more than two such spots are more intense~~  
171 ~~than that obtained with solution E.~~

172 **Dissolution.** Carry out the test described under *5.5 Dissolution test for oral dosage forms*, using as the dissolution medium 1000 mL of hydrochloric acid (~4 g/L) TS and rotating the basket at 100 revolutions per minute. At 45 minutes, withdraw a sample of 10 mL of the medium through an in-line filter. Allow the filtered sample to cool to room temperature.

177 If necessary, dilute a suitable volume of the filtrate with dissolution medium to obtain a solution nominally containing 0.025 mg of dapsone per mL. Measure the absorbance as described under *1.6 Spectrophotometry in the visible and ultraviolet regions* of the resulting solution in a cuvette with an optical pathlength of 10 mm at about 288 nm, using the dissolution medium as the blank.

182 For each of the tablets tested, calculate the total amount of dapsone ( $C_{12}H_{12}N_2O_2S$ ) in the medium using the absorptivity value of 41.5 ( $A_{1\text{cm}}^{1\%} = 415$ ) for dapsone.

184 Evaluate the results as described under *5.5 Dissolution test for solid oral dosage forms, Acceptance criteria*. The amount of dapsone released is not less than 75 % (Q) of the amount declared on the label.

187 **[Note from the Secretariat. It is intended to confirm the absorptivity value of dapsone during the establishment of RS]**

189 **Assay.** Carry out the test as described under *1.14.1 Chromatography, High-performance liquid chromatography*, using a stainless steel column (25 cm x 4.6 mm) packed with end-capped particles of silica gel, the surface of which has been modified with chemically-bonded octadecylsilyl groups (5  $\mu\text{m}$ )<sup>2</sup>.

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<sup>2</sup> An Thermo BDS Hypersil C18Column was found suitable.

193 Use the following conditions for gradient elution:

194 • Mobile phase A: water R.

195 • Mobile phase B: acetonitrile R.

Time (minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comments
0 - 2	80	20	isocratic
2 - 11	80 to 75	20 to 25	linear gradient
11 - 16	75 to 10	25 to 90	linear gradient
16 - 20	10	90	isocratic
20 - 21	10 to 80	90 to 20	return to initial composition
21 - 25	80	20	re-equilibration

196 Operate with a flow rate of 1.0 mL per minute. As a detector, use an ultraviolet spectrophotometer set at a wavelength of 254 nm.

198 Prepare the following solutions using as the diluent a mixture of 50 volumes of water  
199 R and 50 volumes of acetonitrile R.

200 For solution (1), weigh and powder 20 tablets. Transfer a quantity of the powdered  
201 tablets, nominally containing 50.0 mg of dapsone to a 200 mL volumetric flask. Add  
202 170 mL of methanol R, sonicate for 15 minutes at 35 °C with intermittent shaking,  
203 allow to cool to room temperature and add methanol R to volume. Dilute 5.0 mL of  
204 the supernatant to 50.0 mL with diluent and filter. For solution (2), dissolve 50.0 mg  
205 of dapsone RS in 150 mL of methanol R and dilute to 200.0 mL with the same  
206 solvent. Dilute 5.0 mL of this solution to 50.0 mL with diluent.

207 Inject 20 µL each of solutions (1) and (2).

208 Measure the areas of the peaks corresponding to dapsonc obtained in the  
209 chromatograms of solutions (1) and (2) and calculate the percentage content of  
210 dapsone ( $C_{12}H_{12}N_2O_2S$ ) in the tablets, using the declared content of  $C_{12}H_{12}N_2O_2S$  in  
211 dapsone RS.

212 Weigh and powder 20 tablets. Dissolve a quantity of the powder equivalent to about  
213 0.25 g of Dapsone, accurately weighed, in a mixture of 15 mL of water and 15 mL of  
214 hydrochloric acid (~70 g/l) TS. Carry out the assay as described under 2.7 Nitrite  
215 *titration*, titrating with sodium nitrite (0.1 mol/l) VS.

216 Each mL of sodium nitrite (0.1 mol/l) VS is equivalent to 12.42 mg of  $C_{12}H_{12}N_2O_2S$ .

217 **Impurities.** The impurities limited by the requirements of this monograph include  
218 those listed in the monographs on Dapsone

219

220 **Reagents to be established**

221 **4-(4-Aminobenzene-1-sulfonyl)phenol R**

222  $C_{12}H_{11}NO_3S$ .

223 Molecular weight. 249.3

224 Description. Grey or light brown powder, hygroscopic, slightly soluble in methanol.

225 Melting point. About 138 °C.

226 **4-(Benzenesulfonyl)aniline R**

227  $C_{12}H_{11}NO_2S$ .

228 Molecular weight. 233.3

229 Description. Light brown powder.

230 Melting point. About 176 °C.

231 **4,4'-[Oxybis[(4,1-phenylene)sulfonyl]]dianiline R**

232 C<sub>24</sub>H<sub>20</sub>N<sub>2</sub>O<sub>5</sub>S<sub>2</sub>.

233 Molecular weight. 480.6

234 Description. Light brown powder.

235 Melting point. About 220 °C.

236

237 **Reference substance described**

238 **Dapsone RS**

239 ICRS already established, intended uses to be added

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Draft for Comments