World Health Organization

DAPSONE TABLETS (DAPSONI COMPRESSI)

Draft proposal for revision in *The International Pharmacopoeia*

(16 December 2025)

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), with a copy to **Ms Sinéad Jones** (jonessi@who.int, nsp@who.int).
Comments should be submitted through the online platform on or by **16 February 2026**. Please note that only comments received by this deadline will be considered for the preparation of this document.
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SCHEDULE FOR DRAFT WORKING DOCUMENT QAS/23.920

DAPSONE TABLETS (DAPSONI COMPRESSI)

Description	Date
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 59th 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.	

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

Changes are indicated by <u>insert</u> or ~~replace~~.]

DAPSONE TABLETS (DAPSONI COMPRESSI)

Category. Antileprosy medicine.

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

~~The tablets may be coloured.~~

Requirements

Comply with the monograph for *Tablets*.

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

Identity tests

- Either test A, or any two of tests B, C and D, may be applied. ~~Either tests A and B or tests B and C may be applied.~~

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

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

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

Alternatively, 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 230 nm to 350 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 dapsone in the chromatogram obtained with solution (2).

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

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

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

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

Related substances. 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 µm)[1].

Use the following conditions for gradient elution:

- Mobile phase A: water R.
- Mobile phase B: acetonitrile R.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comments
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

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.

[1] An Thermo BDS Hypersil C18Column was found suitable.

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

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

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

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

In the chromatogram obtained with solution (1):

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

- the area of any peak corresponding to impurity A, when multiplied by a correction factor of 1.9, is not greater than 0.3 times the area of the peak due to dapsone in the chromatogram obtained with solution (2) (0.3 %);
- the area of any peak corresponding to impurity C, when multiplied by a correction factor of 1.7, is not greater than 0.3 times the area of the peak due to dapsone in the chromatogram obtained with solution (2) (0.3 %);
- the area of any other impurity peak is not greater than 0.2 times the area of the peak due to dapsone in the chromatogram obtained with solution (2) (0.2 %).
- The sum of the areas of all impurity peaks, including the corrected areas of any peaks corresponding to impurities A, B and C is not greater than 1.5 times the area of the peak due to dapsone in the chromatogram obtained with solution (2) (1.5%). Disregard any peak with an area less than the area of the peak due to dapsone in the chromatogram in the chromatogram obtained with solution (3) (0.1%).

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

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

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.

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.

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 ($A_{1\,cm}^{1\,\%} = 415$) for dapsone.

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.

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

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 µm)[2].

[2] An Thermo BDS Hypersil C18Column was found suitable.

Use the following conditions for gradient elution:

- Mobile phase A: water R.
- 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

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.

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

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

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

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

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

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

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

Reagents to be established

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

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

Molecular weight. 249.3

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

Melting point. About 138 °C.

4-(Benzenesulfonyl)aniline R

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

Molecular weight. 233.3

Description. Light brown powder.

Melting point. About 176 °C.

4,4′-[Oxybis[(4,1-phenylene)sulfonyl]]dianiline R

$C_{24}H_{20}N_2O_5S_2$.

Molecular weight. 480.6

Description. Light brown powder.

Melting point. About 220 °C.

Reference substance described

Dapsone RS

ICRS already established, intended uses to be added

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