World Health Organization

DAPSONE (DAPSONUM)

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/23.919

DAPSONE (DAPSONUM)

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. The revision is based on information found in the public domain and in other pharmacopoeias and submitted by a manufacturer.*

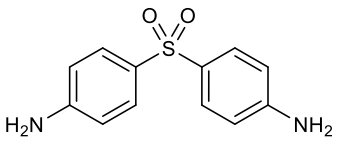
Changes are indicated by insert or ~~replace~~.]

DAPSONE (DAPSONUM)

Molecular formula. $C_{12}H_{12}N_2O_2S$

Relative molecular mass. 248.3

Graphic formula.



Chemical name. 4,4'-Sulfonyldianiline; 4,4'-sulfonylbis[benzenamine]; 4,4'-diaminodiphenylsulfone; CAS Reg. No. 80-08-0.

Description. A white or slightly yellowish-white ~~creamy white~~, crystalline powder~~;~~ ~~odourless~~.

Solubility. Practically insoluble in water R, freely soluble in acetone R, sparingly soluble in ethanol (~750 g/L) TS. It dissolves in dilute mineral acids ~~Soluble in 7000 parts of water and in 30 parts of ethanol (~750 g/l) TS; soluble in acetone R~~.

Category. Antileprotic.

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

Additional information. Even in the absence of light, Dapsone is gradually degraded on exposure to a humid atmosphere, the decomposition being faster at higher temperatures. Dapsone shows polymorphism.

Requirements

Definition. Dapsone contains not less than 99.0% and not more than 101.0% of $C_{12}H_{12}N_2O_2S$, calculated with reference to the dried substance.

Identity tests

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

A. Carry out the test as described under *1.7 Spectrophotometry in the infrared region*. The infrared absorption spectrum is concordant with the spectrum obtained from dapsone RS or with the reference spectrum of dapsone.

If the spectra thus obtained are not concordant, repeat the test using the residues obtained by separately dissolving the test substance and dapson RS in a small amount of acetone R and evaporating to dryness. The infrared absorption spectrum is concordant with the spectrum obtained from dapsone RS.

B. The absorption spectrum of a 5.0 µg/mL solution in methanol R, 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 the maximum wavelength of 260 nm and 295 nm are about 0.36 and 0.60, respectively.

Alternatively, in combination with identity test C, 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 solution (1) given under Related substances. For solution (2), prepare a solution containing 0.4 mg of dapsone RS per mL of a mixture of 50 volumes of water R and 50 volumes of acetonitrile R. 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 R6as 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 in methanol R containing (A) 1 mg of the test substance per mL, and (B) 1 mg of dapsone RS per mL. 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 dapsone in the chromatogram obtained with solution (B). ~~A. The absorption spectrum of a 5.0 µg/mL solution in methanol R, 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 the maximum wavelength of 260 nm and 295 nm are about 0.72 and 1.20, respectively.~~

~~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.~~

E~~C~~. About 0.1 g yields the reaction described for the identification of primary aromatic amines under *2.1 General identification tests*, producing a vivid red precipitate.

~~D. Melting temperature, about 178°C~~.

Sulfated ash. Not more than 1.0 mg/g.

Loss on drying. Dry to constant weight at 105 °C; it loses not more than 15 mg/g.

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.

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), dissolve 40 mg of the test substance in 30 mL and dilute to 100.0 mL. For solution (2), dilute 1.0 mL of the solution (1) to 100.0 mL. For solution (3), dilute 1.0 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).

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

Use the chromatogram obtained with solution (4) to identify the peaks due to 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.

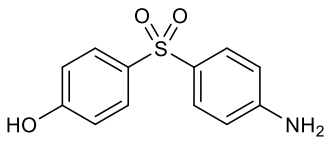
In the chromatogram obtained with solution (1):

- 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 0.1 times the area of the peak due to dapsone in the chromatogram obtained with solution (2) (0.10 %).
- 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 the area of the peak due to dapsone in the chromatogram obtained with solution (2) (1.0%). 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) (0.05%).

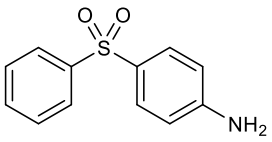
Related substances. Carry out the test as described under 1.14.1 Thin-layer chromatography, but using an unlined chamber, silica gel R3 as the coating substance, and a mixture of 8 volumes of toluene R and 4 volumes of acetone R saturated with water as the mobile phase. Apply separately to the plate 10 µl of each of 5 solutions in methanol R containing (A) 10 mg of the test substance per mL, (B) 10 mg of dapsone RS per mL, (C) 0.15 mg of the test substance per mL, (D) 20 µg of the test substance per mL and (E) 0.10 mg of 4,4' thiodianiline RS per mL. The solution of 4,4' thiodianiline RS should be freshly prepared. Pour the mobile phase into the chamber and insert the plate immediately, to avoid prior saturation of the chamber. After removing the plate from the chromatographic chamber, spray it with 4-dimethylaminocinnamaldehyde TS2. Heat the plate at 100°C and examine the chromatogram in daylight. The spot obtained with solution C is more intense than any spot obtained with solution A, other than the principal spot, and in addition, not more than 2 among those secondary spots are more intense than the spot obtained with solution D. Moreover, there is no visible spot corresponding in position and appearance with that obtained with solution E.

Assay. Carry out the assay as described under *2.7 Nitrite titration*, using about 0.25 0.100 g, accurately weighed, dissolved in a mixture of 15 mL of water and 15 mL of hydrochloric acid (~70 g/L) TS and titrate 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 $C_{12}H_{12}N_2O_2S$.

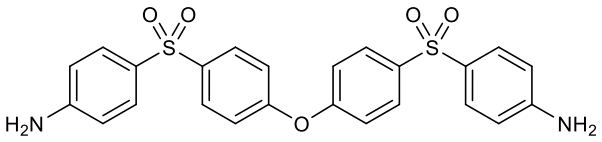
Impurities



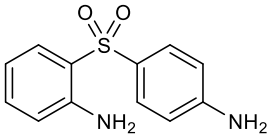
A. 4-(4-Aminobenzene-1-sulfonyl)phenol (synthesis related impurity),



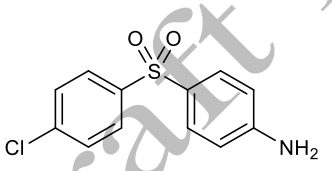
B. 4-(Benzenesulfonyl)aniline (synthesis related impurity),



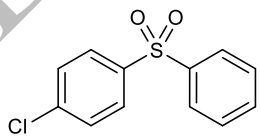
C. $1^4,7^4$-Diamino-$2\lambda^6,6\lambda^6$-4-oxa-2,6-dithia-1,7(1),3,5(1,4)-tetrabenzenaheptaphane-2,2,6,6-tetrone (synthesis related impurity),



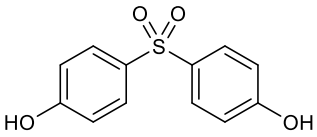
D. 2-(4-Aminobenzene-1-sulfonyl)aniline,

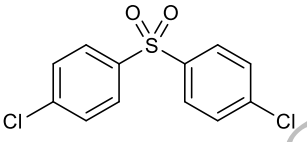


E. 4-(4-Chlorobenzene-1-sulfonyl)aniline,



F. 1-(Benzenesulfonyl)-4-chlorobenzene,



G. 4,4`-Sulfonyldiphenol (synthesis related impurity), 

H. 4,4' dichlorodiphenylsulfone (synthesis related *impurity).*

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 substances described

Dapsone RS

ICRS already established. Intended uses to be adapted.

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