

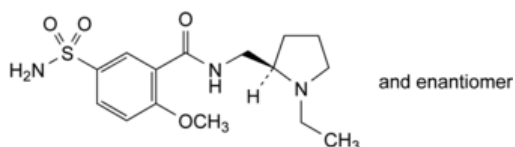


Edition: BP 2025 (Ph. Eur. 11.6 update)

Sulpiride

[General Notices](#)

(Ph. Eur. monograph 1045)



C₁₅H₂₃N₃O₄S 341.4 15676-16-1

Action and use

Dopamine receptor antagonist; neuroleptic.

Preparation

[Sulpiride Tablets](#)

Ph Eur

DEFINITION

N-[[[(2*RS*)-1-Ethylpyrrolidin-2-yl]]methyl]-2-methoxy-5-sulfamoylbenzamide.

Content

98.5 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Practically insoluble in water, sparingly soluble in methanol, slightly soluble in ethanol (96 per cent) and in methylene chloride. It dissolves in dilute solutions of mineral acids and alkali hydroxides.

IDENTIFICATION

First identification: B.

Second identification: A, C, D.

A. Melting point ([2.2.14](#)): 177 °C to 181 °C.

B. Infrared absorption spectrophotometry ([2.2.24](#)).

Comparison [sulpiride CRS](#).

C. Examine the chromatograms obtained in the test for impurity A.

Detection Examine in ultraviolet light at 254 nm.

Results The principal spot in the chromatogram obtained with test solution (b) is similar in position and size to the principal spot in the chromatogram obtained with reference solution (a).

D. To about 1 mg in a porcelain dish, add 0.5 mL of [sulfuric acid R](#) and 0.05 mL of [formaldehyde solution R](#). Examined in ultraviolet light at 365 nm, the solution shows blue fluorescence.

TESTS

Appearance of solution

The solution is clear ([2.2.1](#)) and not more intensely coloured than reference solution Y₆ ([2.2.2, Method I](#)).

Dissolve 1.0 g in [dilute acetic acid R](#) and dilute to 10 mL with the same acid.

Impurity A. Thin-layer chromatography ([2.2.27](#))

Test solution (a) Dissolve 0.20 g of the substance to be examined in [methanol R](#), sonicate until dissolution is complete and dilute to 10.0 mL with the same solvent.

Test solution (b) Dilute 1.0 mL of test solution (a) to 10.0 mL with [methanol R](#).

Reference solution (a) Dissolve 20 mg of [sulpiride CRS](#) in [methanol R](#) and dilute to 10.0 mL with the same solvent.

Reference solution (b) Dissolve 5.0 mg of [sulpiride impurity A CRS](#) in [methanol R](#) and dilute to 25.0 mL with the same solvent. Dilute 1.0 mL of the solution to 10.0 mL with [methanol R](#).

Plate [TLC silica gel F₂₅₄ plate R](#).

Mobile phase [concentrated ammonia R](#), [dioxan R](#), [methanol R](#), [methylene chloride R](#) (2:10:14:90 V/V/V/V).

Application 10 µL.

Development Over 1/2 of the plate.

Drying In air.

Detection Examine in ultraviolet light at 254 nm for identification test C and then spray with [ninhydrin solution R](#); heat at 100-105 °C for 15 min and examine in daylight.

Limit Test solution (a):

— *impurity A*: any spot due to impurity A is not more intense than the corresponding spot in the chromatogram obtained with reference solution (b) (0.1 per cent).

Related substances

Liquid chromatography ([2.2.29](#)).

Test solution Dissolve 0.100 g of the substance to be examined in the mobile phase and dilute to 100.0 mL with the mobile phase.

Reference solution (a) Dilute 1.0 mL of the test solution to 100.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 10.0 mL with the mobile phase.

Reference solution (b) Dissolve 5 mg of the substance to be examined and 5 mg of [sulpiride impurity B CRS](#) in the mobile phase and dilute to 50.0 mL with the mobile phase.

Column:

- size: $l = 0.25\text{ m}$, $\varnothing = 4.6\text{ mm}$;
- stationary phase: [end-capped octylsilyl silica gel for chromatography R](#) (5 μm).

Mobile phase Mix 10 volumes of [acetonitrile R](#), 10 volumes of [methanol R](#) and 80 volumes of a solution containing 6.8 g/L of [potassium dihydrogen phosphate R](#) and 1 g/L of [sodium octanesulfonate R](#), previously adjusted to pH 3.3 with [phosphoric acid R](#).

Flow rate 1.5 mL/min.

Detection Spectrophotometer at 240 nm.

Injection 10 μL .

Run time Twice the retention time of sulpiride.

Identification of impurities Use the chromatogram obtained with reference solution (b) to identify the peak due to impurity B.

Relative retention With reference to sulpiride (retention time = about 15 min): impurity B = about 0.7.

System suitability Reference solution (b):

- **resolution**: minimum 2.5 between the peaks due to impurity B and sulpiride.

Calculation of percentage contents:

- for each impurity, use the concentration of sulpiride in reference solution (a).

Limits:

- **unspecified impurities**: for each impurity, maximum 0.10 per cent;
- **total**: maximum 0.3 per cent;
- **reporting threshold**: 0.05 per cent.

Chlorides (2.4.4)

Maximum 100 ppm.

Shake 1.0 g with 20 mL of [water R](#). Filter through a sintered-glass filter (40) (2.1.2). To 10 mL of the filtrate add 5 mL of [water R](#).

Iron (2.4.9)

Maximum 10 ppm.

Ignite 1.0 g in a silica crucible. To the residue add 1 mL of [1 M hydrochloric acid](#), 3 mL of [water R](#) and 0.1 mL of [nitric acid R](#). Heat on a water-bath for about 5 min. Place the solution in a test-tube. Rinse the crucible with 4 mL of [water R](#). Collect the rinsings in the test-tube and dilute to 10 mL with [water R](#).

Loss on drying (2.2.32)

Maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C.

Sulfated ash (2.4.14)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

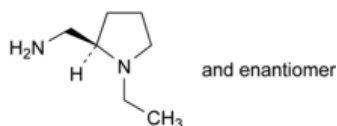
Dissolve 0.250 g in 80 mL of [anhydrous acetic acid R](#). Titrate with [0.1 M perchloric acid](#), determining the end-point potentiometrically (2.2.20).

1 mL of [0.1 M perchloric acid](#) is equivalent to 34.14 mg of $C_{15}H_{23}N_3O_4S$.

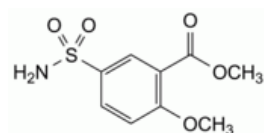
IMPURITIES

Specified impurities A.

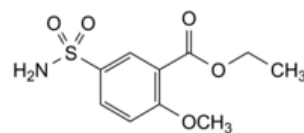
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph [Substances for pharmaceutical use \(2034\)](#). It is therefore not necessary to identify these impurities for demonstration of compliance. See also [5.10. Control of impurities in substances for pharmaceutical use](#)) B, C, D, E, F, G.



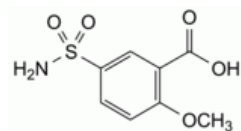
A. [(2RS)-1-ethylpyrrolidin-2-yl]methanamine,



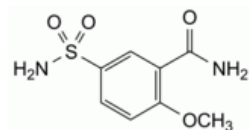
B. methyl 2-methoxy-5-sulfamoylbenzoate,



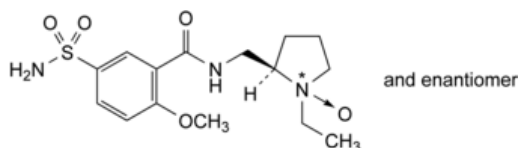
C. ethyl 2-methoxy-5-sulfamoylbenzoate,



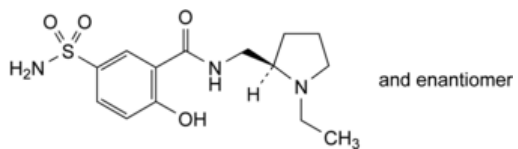
D. 2-methoxy-5-sulfamoylbenzoic acid,



E. 2-methoxy-5-sulfamoylbenzamide,



F. *N*-[[[(2RS)-1-ethyl-1-oxidopyrrolidin-2-yl]methyl]-2-methoxy-5-sulfamoylbenzamide,



G. *N*-[[*(2RS)*-1-éthylpyrrolidin-2-yl]méthyl]-2-hydroxy-5-sulfamoylbenzamide.

Ph Eur



Edition: BP 2025 (Ph. Eur. 11.6 update)

Sulpiride Tablets

[General Notices](#)

Action and use

Dopamine receptor antagonist; neuroleptic.

DEFINITION

Sulpiride Tablets contain Sulpiride.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of sulpiride, $C_{15}H_{23}N_3O_4S$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

To a quantity of the powdered tablets containing 0.2 g of Sulpiride add 20 mL of [methanol](#), shake for 5 minutes, filter and evaporate the filtrate to dryness. The [infrared absorption spectrum](#) of the residue, [Appendix II A](#), is concordant with the *reference spectrum* of sulpiride ([RS 391](#)).

Related substances

- A. Carry out the method for [thin-layer chromatography](#), [Appendix III A](#), using the following solutions.
- (1) Add 20 mL of [methanol](#) to a quantity of the powdered tablets containing 0.2 g of Sulpiride, shake for 5 minutes, filter, evaporate the filtrate to dryness and dissolve the residue in 10 mL of [methanol](#).
 - (2) 0.02% w/v of [sulpiride impurity A EPCRS](#) in [methanol](#).
 - (3) Dilute 1 volume of solution (2) to 10 volumes with [methanol](#).

CHROMATOGRAPHIC CONDITIONS

- Use a [silica gel HF₂₅₄](#) precoated plate (Analtech Uniplates are suitable).
- Use the mobile phase as described below.
- Apply 10 µL of each solution.
- Develop the plate to 10 cm.
- After removal of the plate, dry in air, spray with [ninhydrin solution](#) and heat at 100° to 105° for 15 minutes.

MOBILE PHASE

2 volumes of 13.5M [ammonia](#), 10 volumes of [1,4-dioxan](#), 14 volumes of [methanol](#) and 90 volumes of [dichloromethane](#).

LIMITS

Any spot in the chromatogram obtained with solution (1) corresponding to the principal spot in the chromatogram obtained with solution (2) is not more intense than the spot in the chromatogram obtained with solution (3) (0.1%).

B. Carry out the method for [liquid chromatography](#), [Appendix III D](#), using the following solutions.

- (1) Add 20 mL of [methanol](#) to a quantity of the powdered tablets containing 0.2 g of Sulpiride, shake for 5 minutes, filter, evaporate the filtrate to dryness and dissolve the residue in sufficient of the mobile phase to produce 200 mL.
- (2) Dilute 3 volumes of solution (1) to 100 volumes with the mobile phase and dilute 1 volume of this solution to 10 volumes with the mobile phase.
- (3) 0.01% w/v of [sulpiride BPCRS](#) and 0.01% w/v of [sulpiride impurity B EPCRS](#) in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

- (a) Use a stainless steel column (25 cm × 4.6 mm) packed with [octylsilyl silica gel for chromatography](#) (5 µm) (Zorbax RX C8 is suitable).
- (b) Use isocratic elution and the mobile phase described below.
- (c) Use a flow rate of 1.5 mL per minute.
- (d) Use an ambient column temperature.
- (e) Use a detection wavelength of 240 nm.
- (f) Inject 20 µL of each solution.
- (g) For solution (1) and solution (2) allow the chromatography to proceed for 2.5 times the retention time of sulpiride.

MOBILE PHASE

10 volumes of [acetonitrile](#), 10 volumes of [methanol](#) and 80 volumes of a solution containing 0.68 % w/v of [potassium dihydrogen orthophosphate](#) and 0.1% w/v of [sodium octanesulfonate](#), adjusted to pH 3.3 using [orthophosphoric acid](#).

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the [resolution factor](#) between the two principal peaks is at least 2.5.

LIMITS

In the chromatogram obtained with solution (1):

the sum of the areas of any [secondary peaks](#) is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.3%).

ASSAY

Weigh and powder 20 tablets. Mix a quantity of the powder containing 0.1 g of Sulpiride with about 50 mL of 0.1M [sodium hydroxide](#) for 5 minutes with the aid of ultrasound, add sufficient 0.1M [sodium hydroxide](#) to produce 100 mL and filter, discarding the first 10 mL of filtrate. Dilute 5 mL of the filtrate to 100 mL with 0.1M [sodium hydroxide](#) and measure the [absorbance](#) of the solution at the maximum at 291 nm, [Appendix II B](#), using 0.1M [sodium hydroxide](#) in the reference cell. Calculate the content of C₁₅H₂₃N₃O₄S in the tablets from the [absorbance](#) of a 0.005% w/v solution of [sulpiride BPCRS](#) in 0.1M [sodium hydroxide](#) using the declared content of C₁₅H₂₃N₃O₄S in [sulpiride BPCRS](#).

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Sulpiride.