ASSAY

Dissolve 0.300 g in 50 mL of *methanol R*. Titrate with *0.1 M sodium hydroxide*, determining the end-point potentiometrically (*2.2.20*).

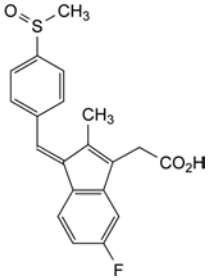
1 mL of *0.1 M sodium hydroxide* is equivalent to 35.64 mg of $C_{20}H_{17}FO_3S$.

STORAGE

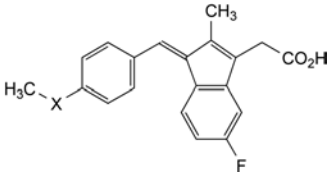
Protected from light.

IMPURITIES

Specified impurities: *A, B, C.*



A. (*E*)-[5-fluoro-2-methyl-1-[4-(methylsulfinyl)benzylidene]-1*H*-inden-3-yl]acetic acid,



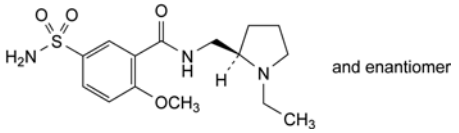
B. X = SO_2: (*Z*)-[5-fluoro-2-methyl-1-[4-(methylsulfonyl)-benzylidene]-1*H*-inden-3-yl]acetic acid,

C. X = S: (*Z*)-[5-fluoro-2-methyl-1-[4-methylsulfanyl)-benzylidene]-1*H*-inden-3-yl]acetic acid.

01/2008:1045
corrected 6.0

SULPIRIDE

Sulpiridum



$C_{15}H_{23}N_3O_4S$ M_r 341.4
[15676-16-1]

DEFINITION

(*RS*)-*N*-[(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: *A, B.*

Second identification: *A, C, D.*

A. Melting point (*2.2.14*): 177 °C to 181 °C.

B. Infrared absorption spectrophotometry (*2.2.24*).
Preparation: discs.
Comparison: *sulpiride CRS.*

C. Examine the chromatograms obtained in test A for related substances.
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 Y_6 (*2.2.2, Method I*).

Dissolve 1.0 g in *dilute acetic acid R* and dilute to 10 mL with the same acid.

Related substances

A. Thin-layer chromatography (*2.2.27*).
Test solution (a). Dissolve 0.20 g of the substance to be examined in *methanol R* and dilute to 10 mL with the same solvent. Sonicate until complete dissolution.
Test solution (b). Dilute 1 mL of test solution (a) to 10 mL with *methanol R*.
Reference solution (a). Dissolve 20 mg of *sulpiride CRS* in *methanol R* and dilute to 10 mL with the same solvent.
Reference solution (b). Dissolve 5 mg of *sulpiride impurity A CRS* in *methanol R* and dilute to 25 mL with the same solvent.
Reference solution (c). Dilute 1.0 mL of reference solution (b) to 10 mL with *methanol R*.
Plate: *TLC silica gel F_{254} 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 a path of 10 cm.
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 (c) (0.1 per cent).

B. 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 3.0 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 10 mg of *sulpiride CRS* and 10 mg of *sulpiride impurity B CRS* in the mobile phase and dilute to 100.0 mL with the mobile phase.
Column:
– *size*: *l* = 0.25 m, Ø = 4.6 mm;
– *stationary phase*: *octylsilyl silica gel for chromatography R* (5 µm) in spherical micro-particles.
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*, adjusted to pH 3.3 using *phosphoric acid R*.
Flow rate: 1.5 mL/min.

Detection: spectrophotometer at 240 nm.

Injection: 10 µL.

Run time: 2.5 times the retention time of sulpiride.

System suitability: reference solution (b):

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

Limit:

– *total*: not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.3 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 a few minutes. 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*.

Heavy metals (*2.4.8*): maximum 10 ppm.

1.0 g complies with test C. Prepare the reference solution using 1 mL of *lead standard solution (10 ppm Pb) 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

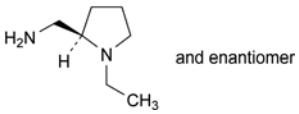
Dissolve 0.250 g in 80 mL of *anhydrous acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M perchloric acid* is equivalent to 34.14 mg of $C_{15}H_{23}N_3O_4S$.

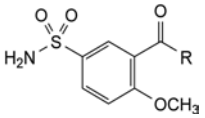
IMPURITIES

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

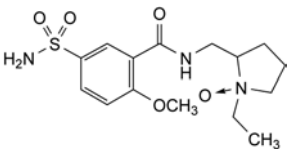


B. R = O-CH_3: methyl 2-methoxy-5-sulfamoylbenzoate,

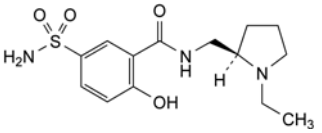
C. R = O-C_2H_5: ethyl 2-methoxy-5-sulfamoylbenzoate,

D. R = OH: 2-methoxy-5-sulfamoylbenzoic acid,

E. R = NH_2: 2-methoxy-5-sulfamoylbenzamide,



F. 1-ethyl-2-[[(2-methoxy-5-sulfamoylbenzoyl)amino]-methyl]pyrrolidine 1-oxide,

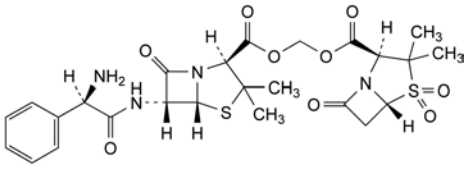


G. (*RS*)-*N*-[(1-ethylpyrrolidin-2-yl)methyl]-2-hydroxy-5-sulfamoylbenzamide.

04/2008:2211

SULTAMICILLIN

Sultamicillinum



$C_{25}H_{30}N_4O_9S_2$ M_r 594.7

[76497-13-7]

DEFINITION

Methylene (2*S*,5*R*,6*R*)-6-[[(2*R*)-aminophenylacetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate (2*S*,5*R*)-3,3-dimethyl-4,4,7-trioxo-4λ⁶-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate.

Semi-synthetic product derived from a fermentation product.

Content: 96.0 per cent to 102.0 per cent (anhydrous substance).

CHARACTERS

Appearance: white or almost white, slightly hygroscopic, crystalline powder.

Solubility: practically insoluble in water, very slightly soluble in methanol, practically insoluble in ethanol (96 per cent).

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *sultamicillin CRS*.

TESTS

Specific optical rotation (*2.2.7*): + 190 to + 210 (anhydrous substance).

Dissolve 0.500 g in *dimethylformamide R* and dilute to 50.0 mL with the same solvent.

Related substances. Liquid chromatography (*2.2.29*). *Prepare the solutions immediately before use or keep at 2-8 °C for not more than 6 h.*

Solution A: *methanol R1, acetonitrile R1* (20:80 *V/V*).

Solution B. Dissolve 1.56 g of *sodium dihydrogen phosphate R* in 900 mL of *water R*. Add 7.0 mL of *phosphoric acid R* and dilute to 1000 mL with *water R*.

Blank solution: solution B, solution A (30:70 *V/V*).

Test solution. Dissolve 50.0 mg of the substance to be examined in 35 mL of solution A and sonicate for about 1 min. Add 13 mL of solution B, mix and sonicate for about 1 min. Dilute to 50.0 mL with solution B and mix.