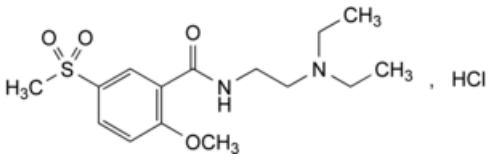
Edition: BP 2025 (Ph. Eur. 11.6 update)

Tiapride Hydrochloride

General Notices

(Ph. Eur. monograph 1575)



$C_{15}H_{25}ClN_2O_4S$ 364.9 *51012-33-0*

Action and use

Dopamine receptor antagonist; neuroleptic.

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DEFINITION

N-[2-(Diethylamino)ethyl]-2-methoxy-5-(methylsulfonyl)benzamide hydrochloride.

Content

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

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Very soluble in water, soluble in methanol, slightly soluble in anhydrous ethanol.

IDENTIFICATION

A. Infrared absorption spectrophotometry (2.2.24).

Comparison *tiapride hydrochloride CRS*.

B. Solution S (see Tests) gives reaction (a) of chlorides (2.3.1).

TESTS

Solution S

Dissolve 2.5 g in *carbon dioxide-free water R* and dilute to 50.0 mL with the same solvent.

Appearance of solution

Solution S is clear (*2.2.1*) and its absorbance (*2.2.25*) at 450 nm is not greater than 0.030.

pH (*2.2.3*)

4.0 to 6.0 for solution S.

Impurity C

Thin-layer chromatography (*2.2.27*).

Test solution Dissolve 0.400 g of the substance to be examined in *methanol R* and dilute to 10 mL with the same solvent.

Reference solution Dissolve 20.0 mg of *metoclopramide impurity E CRS* (impurity C) in *methanol R* and dilute to 50 mL with the same solvent. Dilute 2.0 mL of the solution to 20 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 4/5 of the plate.

Drying In air.

Detection Spray with a 2 g/L solution of *ninhydrin R* in *butanol R* and heat at 100 °C for 15 min.

Retardation factors Impurity C = about 0.1; tiapride = about 0.6.

Limit:

— *impurity C*: any spot due to impurity C is not more intense than the corresponding spot in the chromatogram obtained with the reference solution (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 10.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 100.0 mL with the mobile phase.

Reference solution (b) Dissolve 5.0 mg of *tiapride hydrochloride CRS* and 5.0 mg of *tiapride N-oxide CRS* (impurity D) 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*: *base-deactivated end-capped octylsilyl silica gel for chromatography R* (5 µm);

— *temperature*: 40 °C.

Mobile phase Dissolve 5.44 g of *potassium dihydrogen phosphate R* and 0.08 g of *sodium octanesulfonate R* in 780 mL of *water R*, adjust to pH 2.7 with *phosphoric acid R* and dilute to 800 mL with *water R*; add 150 mL of *methanol R* and 50 mL of *acetonitrile R* and mix.

Flow rate 1.5 mL/min.

Detection Spectrophotometer at 240 nm.

Injection 10 µL.

Run time 3 times the retention time of tiapride.

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

Relative retention With reference to tiapride (retention time = about 7 min): impurity D = about 1.2.

System suitability Reference solution (b):

— *resolution*: minimum 4.0 between the peaks due to tiapride and impurity D.

Calculation of percentage contents:

— for each impurity, use the concentration of tiapride hydrochloride in reference solution (a).

Limits:

— *unspecified impurities*: for each impurity, maximum 0.10 per cent;

— *total*: maximum 0.2 per cent;

— *reporting threshold*: 0.05 per cent.

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

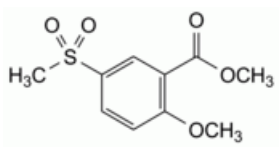
Dissolve 0.300 g in 20 mL of *anhydrous acetic acid R*. Add 20 mL of *acetic anhydride R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M perchloric acid* is equivalent to 36.49 mg of $C_{15}H_{25}ClN_2O_4S$.

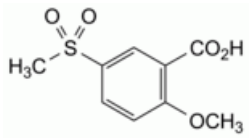
IMPURITIES

Specified impurities *C*.

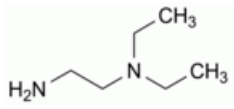
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical 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) *A, B, D*.



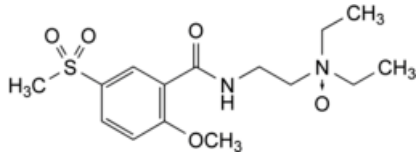
A. methyl 2-methoxy-5-(methylsulfonyl)benzoate,



B. 2-methoxy-5-(methylsulfonyl)benzoic acid,



C. *N*,*N*-diethylethane-1,2-diamine,



D. *N*-[2-(diethyloxidoaminol)ethyl]-2-methoxy-5-(methylsulfonyl)benzamide (tiapride *N*-oxide).

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