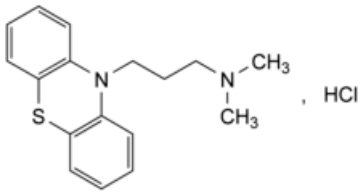
Edition: BP 2025 (Ph. Eur. 11.6 update)

Promazine Hydrochloride

General Notices

(Ph. Eur. monograph 1365)



$C_{17}H_{21}ClN_2S$ 320.9 *53-60-1*

Action and use

Dopamine receptor antagonist; neuroleptic.

Preparations

Promazine Injection

Promazine Tablets

Ph Eur

DEFINITION

N,*N*-Dimethyl-3-(10*H*-phenothiazin-10-yl)propan-1-amine hydrochloride.

Content

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

CHARACTERS

Appearance

White or almost white, slightly hygroscopic, crystalline powder.

Solubility

Very soluble in water, in ethanol (96 per cent) and in methylene chloride.

mp

About 179 °C.

IDENTIFICATION

First identification: A, D.

Second identification: B, C, D.

A. Infrared absorption spectrophotometry (2.2.24).
Comparison: promazine hydrochloride CRS.
B. Identification test for phenothiazines by thin-layer chromatography (2.3.3): use promazine hydrochloride CRS to prepare the reference solution.
C. Dissolve about 5 mg in 2 mL of sulfuric acid R and allow to stand for 5 min. An orange colour is produced.
D. Dissolve 18 mg in 2 mL of methanol R. The solution gives reaction (a) of chlorides (2.3.1).

TESTS

pH (2.2.3)

4.2 to 5.2, measured immediately after preparation.

Dissolve 0.5 g in carbon dioxide-free water R and dilute to 10 mL with the same solvent.

Related substances

Liquid chromatography (2.2.29). *Use freshly prepared solutions and protect from light*.

Buffer solution Dissolve 1.2 g of ammonium hydrogen carbonate R in water for chromatography R and dilute to 1000 mL with water for chromatography R. Adjust to pH 10.8 with ammonia R.

Test solution Dissolve 60.0 mg of the substance to be examined in mobile phase A and dilute to 50.0 mL with mobile phase A.

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

Reference solution (b) Dissolve 6 mg of promazine impurity B CRS and 6 mg of promazine impurity C CRS in mobile phase A, using sonication if necessary, and dilute to 100 mL with mobile phase A. Dilute 1 mL of the solution to 50 mL with mobile phase A.

Column:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

— *stationary phase*: end-capped octadecylsilyl silica gel for chromatography R (5 µm);

— *temperature*: 30 °C.

Mobile phase:

— *mobile phase A*: buffer solution, acetonitrile R (35:50 *V/V*);

— *mobile phase B*: buffer solution, acetonitrile R (10:90 *V/V*);

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 22	100	0
22 - 37	100 → 0	0 → 100
37 - 60	0	100

Flow rate 1.0 mL/min.

Detection Spectrophotometer at 254 nm.

Injection 10 µL.

Identification of peaks Use the chromatogram obtained with reference solution (b) to identify the peaks due to impurities B and C.

Relative retention With reference to promazine (retention time = about 22 min): impurity C = about 0.56; impurity B = about 0.68. The elution order of impurities C and B may be inverted.

System suitability Reference solution (b):

— *resolution*: minimum 1.5 between the peaks due to impurities C and B.

Calculation of percentage content:

— use the concentration of promazine hydrochloride 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.

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 a mixture of 5.0 mL of *0.01 M hydrochloric acid* and 50 mL of *ethanol (96 per cent) R*. Carry out a potentiometric titration (*2.2.20*), using *0.1 M sodium hydroxide*. Read the volume added between the 2 points of inflexion.

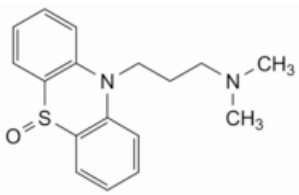
1 mL of *0.1 M sodium hydroxide* is equivalent to 32.09 mg of $C_{17}H_{21}ClN_2S$.

STORAGE

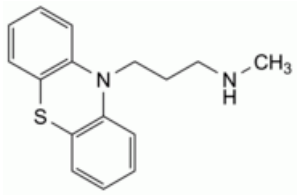
In an airtight container protected from light.

IMPURITIES

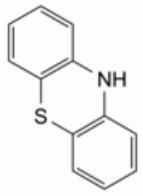
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph *Substances for pharmaceutical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



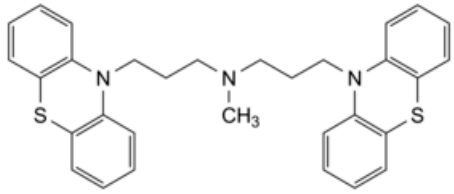
A. 10-[3-(dimethylamino)propyl]-5λ^4-phenothiazin-5(10*H*)-one (promazine sulfoxide),



B. *N*-methyl-3-(10*H*-phenothiazin-10-yl)propan-1-amine,



C. 10*H*-phenothiazine,



D. *N*-methyl-3-(10*H*-phenothiazin-10-yl)-*N*-[3-(10*H*-phenothiazin-10-yl)propyl]propan-1-amine.

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