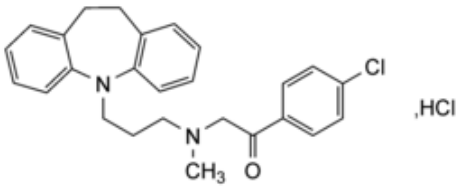
Edition: BP 2025 (Ph. Eur. 11.6 update)

Lofepramine Hydrochloride

General Notices



$C_{26}H_{27}ClN_2O,HCl$ 455.4 *26786-32-3*

Action and use

Monoamine reuptake inhibitor; tricyclic antidepressant.

Preparation

Lofepramine Tablets

DEFINITION

Lofepramine Hydrochloride is 5-(3-[*N*-(4-chlorophenacyl)-*N*-methylamino]propyl)10,11-dihydro-5*H*-dibenz[*b,f*]azepine hydrochloride. It contains not less than 98.5% and not more than 101.0% of $C_{26}H_{27}ClN_2O,HCl$, calculated with reference to the dried substance.

CHARACTERISTICS

A fine, yellowish white to greenish yellow powder.

Very soluble in *ethanol (96%)* and in *methanol*; slightly soluble in *acetone*; very slightly soluble in *water*.

It exhibits polymorphism.

IDENTIFICATION

A. The *infrared absorption spectrum*, Appendix II A, is concordant with the reference spectrum of *lofepramine hydrochloride (form A) (RS 399A)*.
B. 2 mL of a 1% w/v solution in *ethanol (96%)* complies with the test for *chlorides*, Appendix VI.

TESTS

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions. Solution (1) contains 0.1% w/v of the substance being examined in the mobile phase. For solution (2) dilute 1 volume of solution (1) to 200 volumes with the mobile phase. Solution (3) contains 0.0002% w/v each of *desipramine hydrochloride BPCRS* and *imipramine hydrochloride BPCRS* in the mobile phase.

Inject 20 µL of solutions (1) and (2). Inject 20 µL of solution (3) and allow the chromatography to continue for 4 times the retention time of the principal peak.

The chromatographic procedure may be carried out using (a) a stainless steel column (25 cm × 4.6 mm) packed with *base-deactivated end-capped octylsilyl silica gel for chromatography* (5 µm) (Lichrospher 60 RP-select B is suitable) maintained at 50°, (b) as the mobile phase with a flow rate of 1.5 mL per minute a 0.09% w/v solution of *sodium dodecyl sulfate* in a mixture of 550 volumes of *acetonitrile*, 325 volumes of *water* and 125 volumes of a buffer solution of pH 1.0 containing 0.015% w/v of *glycine*, 0.018% w/v of *sodium chloride* and 0.44% w/v of *hydrochloric acid* and (c) a detection wavelength of 254 nm.

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution factor* between the two principal peaks is at least 0.9.

In the chromatogram obtained with solution (1) the area of any *secondary peak* is not greater than the area of the peak in the chromatogram obtained with solution (2) (0.5%) and the sum of the areas of any *secondary peaks* is not greater than twice the area of the peak in the chromatogram obtained with solution (2) (1%).

Loss on drying

When dried at a temperature of 100° at a pressure not exceeding 0.2 kPa, loses not more than 0.5% of its weight. Use 1 g.

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions. Solution (1) contains 0.02% w/v of the substance being examined in the mobile phase. Solution (2) contains 0.02% w/v of *lofepramine hydrochloride BPCRS* in the mobile phase.

The chromatographic procedure described under the test for Related substances may be used.

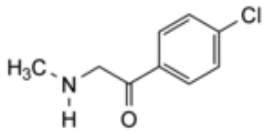
Inject 20 µL of each solution.

Calculate the content of $C_{26}H_{27}ClN_2O$,HCl from the chromatograms obtained and using the declared content of $C_{26}H_{27}ClN_2O$,HCl in *lofepramine hydrochloride BPCRS*.

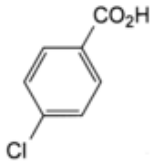
STORAGE

Lofepramine Hydrochloride should be kept in an airtight container and protected from light.

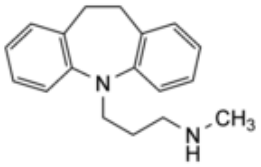
IMPURITIES



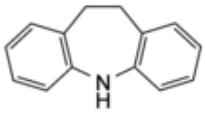
A. 1-methylamino-4′-chloroacetophenone,



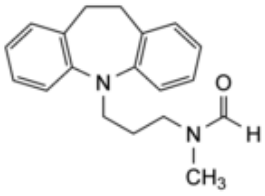
B. 4-chlorobenzoic acid,



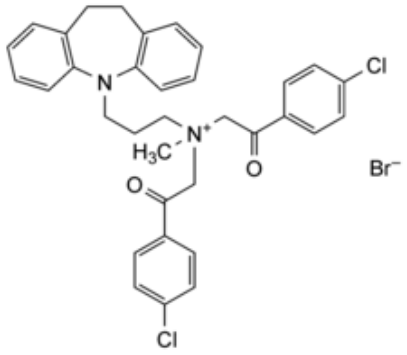
C. desipramine,



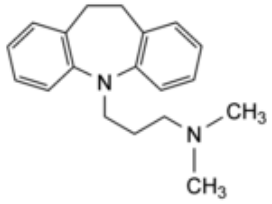
D. iminodibenzyl,



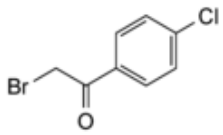
E. *N*-formyldesipramine,



F. *N,N*-bis(4′-chlorophenacyl)desipramine bromide,



G. imipramine,



H. 2-bromo-4′-chloroacetophenone.