

System suitability: reference solution (b):

- *resolution*: minimum 2.0 between the peaks due to impurities A and B.

Limits:

- *impurities A, B, C*: for each impurity, not more than the area of the corresponding peak in the chromatogram obtained with reference solution (b) (0.1 per cent);
- *any other impurity*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent);
- *total*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent);
- *disregard limit*: 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.01 per cent).

Loss on drying (2.2.32): maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 80 °C for 3 h.

Sulfated ash (2.4.14): maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.250 g in 50 mL of *anhydrous acetic acid R*. Titrate with 0.1 M *perchloric acid*, determining the end-point potentiometrically (2.2.20).

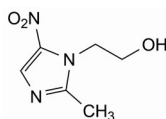
1 mL of 0.1 M *perchloric acid* is equivalent to 27.53 mg of C₁₃H₁₃N₃O₄.

STORAGE

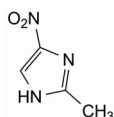
Protected from light.

IMPURITIES

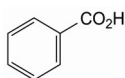
Specified impurities: A, B, C.



- A. 2-(2-methyl-5-nitro-1H-imidazol-1-yl)ethanol (metronidazole),



- B. 2-methyl-4-nitroimidazole,



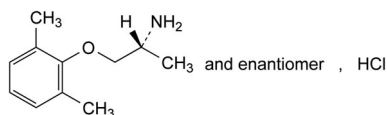
- C. benzenecarboxylic acid (benzoic acid).



01/2021:1029

MEXILETINE HYDROCHLORIDE

Mexiletini hydrochloridum



C₁₁H₁₈ClNO
[5370-01-4]

M_r 215.7

DEFINITION

(2RS)-1-(2,6-Dimethylphenoxy)propan-2-amine hydrochloride.

Content: 99.0 per cent to 101.0 per cent (anhydrous substance).

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: freely soluble in water and in methanol, sparingly soluble in methylene chloride.

It shows polymorphism (5.9).

IDENTIFICATION

- A. Infrared absorption spectrophotometry (2.2.24).

Comparison: *mexiletine hydrochloride CRS*.

If the spectra obtained in the solid state show differences, dissolve the substance to be examined and the reference substance separately in *methanol R*, evaporate to dryness and record new spectra using the residues.

- B. Dilute 1.5 mL of solution S (see Tests) to 15 mL with *water R*. The solution gives reaction (a) of chlorides (2.3.1).

TESTS

Solution S. Dissolve 2.0 g in *carbon dioxide-free water R* and dilute to 20 mL with the same solvent.

Appearance of solution. The solution is clear (2.2.1) and colourless (2.2.2, *Method II*).

Dilute 5 mL of solution S to 10 mL with *water R*.

pH (2.2.3): 4.0 to 5.5 for solution S.

Impurity D. Liquid chromatography (2.2.29).

Buffer solution. To 1790 mL of *water for chromatography R* add 15 mL of *triethylamine R* and 1 mL of *glacial acetic acid R*.

Solvent mixture: *acetonitrile R*, *water R* (20:80 V/V).

Test solution. Dissolve 0.200 g of the substance to be examined in the solvent mixture and dilute to 10.0 mL with the solvent mixture.

Reference solution (a). Dissolve 5.0 mg of *mexiletine impurity D CRS* in the solvent mixture and dilute to 25.0 mL with the solvent mixture.

Reference solution (b). Dilute 1.0 mL of reference solution (a) to 10.0 mL with the solvent mixture.

Reference solution (c). Mix 1 mL of reference solution (a) and 1 mL of the test solution and dilute to 10 mL with the solvent mixture.

Column:

- *size*: $l = 0.25$ m, $\varnothing = 4.6$ mm;
- *stationary phase*: *end-capped ethylene-bridged octadecylsilyl silica gel for chromatography (hybrid material) R* (5 μ m);
- *temperature*: 40 °C.

Mobile phase: *acetonitrile R*, buffer solution (18:82 V/V); adjust to pH 11.5 with *triethylamine R*.

Flow rate: 2.0 mL/min.

Detection: spectrophotometer at 262 nm.

Injection: 30 μ L of the test solution and reference solutions (b) and (c).

Run time: twice the retention time of mexiletine.

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

Relative retention with reference to mexiletine (retention time = about 26 min): impurity D = about 0.9.

System suitability: reference solution (c):

- *resolution*: minimum 1.5 between the peaks due to impurity D and mexiletine.

Calculation of percentage content:

- for impurity D, use the concentration of impurity D in reference solution (b).

Limit:

- impurity D: maximum 0.10 per cent.

Related substances. Liquid chromatography (2.2.29).

Test solution. Dissolve 0.200 g of the substance to be examined in the mobile phase and dilute to 10.0 mL with the mobile phase.

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

Reference solution (b). Dissolve 2.0 mg of *mexiletine impurity C CRS* in the mobile phase and transfer the solution quantitatively to a volumetric flask containing 16.0 mg of *mexiletine impurity A CRS*, then dilute to 20.0 mL with the mobile phase. Mix 1.0 mL of this solution with 2.0 mL of reference solution (a) and dilute the mixture to 100.0 mL with the mobile phase.

Column:

- size: $l = 0.25$ m, $\varnothing = 4.6$ mm;
- stationary phase: end-capped octadecylsilyl silica gel for chromatography R (5 μ m).

Mobile phase: mix 65 volumes of *methanol R2* and 35 volumes of a solution prepared as follows: dissolve 11.5 g of *anhydrous sodium acetate R* in 500 mL of *water for chromatography R*, add 3.2 mL of *glacial acetic acid R*, mix and allow to cool; adjust to pH 4.8 with *glacial acetic acid R* and dilute to 1000 mL with *water for chromatography R*.

Flow rate: 1.0 mL/min.

Detection: spectrophotometer at 262 nm.

Injection: 20 μ L.

Run time: 5.5 times the retention time of *mexiletine*.

Identification of impurities: use the chromatogram obtained with reference solution (b) to identify the peaks due to impurities A and C.

Relative retention with reference to *mexiletine* (retention time = about 4 min): impurity C = about 0.7; impurity A = about 1.8.

System suitability: reference solution (b):

- resolution: minimum 5.0 between the peaks due to impurity C and *mexiletine*.

Limits:

- impurity A: not more than 2.5 times the area of the corresponding peak in the chromatogram obtained with reference solution (b) (0.10 per cent);
- impurity C: not more than 20 times the area of the corresponding peak in the chromatogram obtained with reference solution (b) (0.10 per cent);
- unspecified impurities: for each impurity, not more than 0.5 times the area of the peak due to *mexiletine* in the chromatogram obtained with reference solution (b) (0.10 per cent);
- total: not more than 2.5 times the area of the peak due to *mexiletine* in the chromatogram obtained with reference solution (b) (0.5 per cent);
- disregard limit: 0.25 times the area of the peak due to *mexiletine* in the chromatogram obtained with reference solution (b) (0.05 per cent).

Water (2.5.12): maximum 0.5 per cent, determined on 1.00 g.

Sulfated ash (2.4.14): maximum 0.1 per cent, determined on 1.0 g.

ASSAY

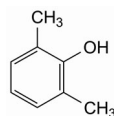
Dissolve 0.150 g in 50 mL of a mixture of equal volumes of *acetic anhydride R* and *anhydrous acetic acid R*. Titrate immediately with 0.1 M *perchloric acid*, determining the end-point potentiometrically (2.2.20) and completing the titration within 2 min.

1 mL of 0.1 M *perchloric acid* is equivalent to 21.57 mg of $C_{11}H_{18}ClNO$.

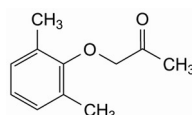
IMPURITIES

Specified impurities: A, C, D.

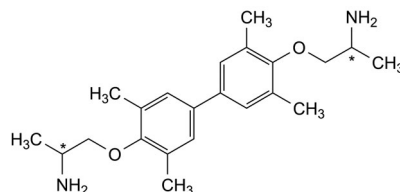
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph *Substances for pharmaceutical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



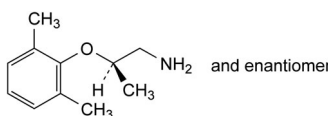
A. 2,6-dimethylphenol,



B. 1-(2,6-dimethylphenoxy)propan-2-one,



C. 1,1'-[(3,3',5,5'-tetramethyl[1,1'-biphenyl]-4,4'-diyl)bis(oxy)]di(propan-2-amine),



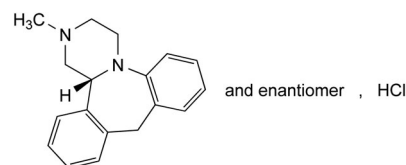
D. (2*RS*)-2-(2,6-dimethylphenoxy)propan-1-amine.

07/2015:0846
corrected 10.0



MIANSERIN HYDROCHLORIDE

Mianserini hydrochloridum



$C_{18}H_{21}ClN_2$
[21535-47-7]

M_r 300.8

DEFINITION

(14*bRS*)-2-Methyl-1,2,3,4,10,14*b*-hexahydrodibenzo-*[c,f]*pyrazino[1,2-*a*]azepine hydrochloride.

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

CHARACTERS

Appearance: white or almost white, crystalline powder or crystals.

Solubility: sparingly soluble in water and in methylene chloride, slightly soluble in ethanol (96 per cent).