ASSAY

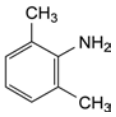
To 0.200 g add 50 mL of *anhydrous acetic acid R* and stir until dissolution is complete. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M perchloric acid* is equivalent to 23.43 mg of $C_{14}H_{22}N_2O$.

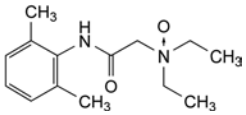
IMPURITIES

Specified impurities: *A*.

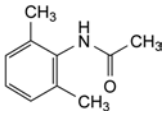
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph *Substances for pharmaceutical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



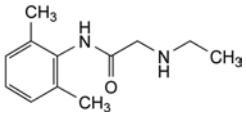
A. 2,6-dimethylaniline,



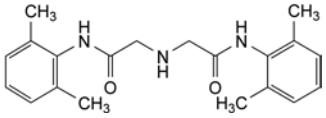
B. 2-(diethylazinoyl)-*N*-(2,6-dimethylphenyl)acetamide (lidocaine *N*-oxide),



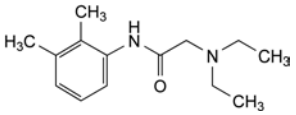
C. *N*-(2,6-dimethylphenyl)acetamide,



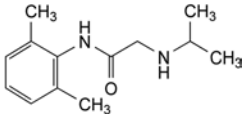
D. *N*-(2,6-dimethylphenyl)-2-(ethylamino)acetamide,



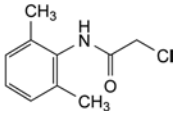
E. 2,2′-iminobis(*N*-(2,6-dimethylphenyl)acetamide),



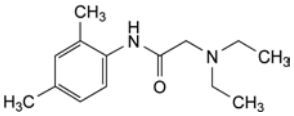
F. 2-(diethylamino)-*N*-(2,3-dimethylphenyl)acetamide,



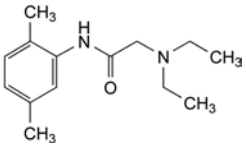
G. *N*-(2,6-dimethylphenyl)-2-((1-methylethyl)amino) acetamide,



H. 2-chloro-*N*-(2,6-dimethylphenyl)acetamide,



I. 2-(diethylamino)-*N*-(2,4-dimethylphenyl)acetamide,

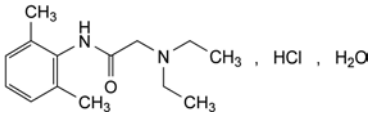


J. 2-(diethylamino)-*N*-(2,5-dimethylphenyl)acetamide.

01/2008:0227

LIDOCAINE HYDROCHLORIDE

Lidocaini hydrochloridum



$C_{14}H_{23}ClN_2O,H_2O$ M_r 288.8
[6108-05-0]

DEFINITION

2-(Diethylamino)-*N*-(2,6-dimethylphenyl)acetamide hydrochloride monohydrate.

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

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: very soluble in water, freely soluble in ethanol (96 per cent).

IDENTIFICATION

First identification: *B, D.*

Second identification: *A, C, D.*

A. Melting point (*2.2.14*): 74 °C to 79 °C, determined without previous drying.

B. Infrared absorption spectrophotometry (*2.2.24*).
Comparison: *lidocaine hydrochloride CRS*.

C. To about 5 mg add 0.5 mL of *fuming nitric acid R*. Evaporate to dryness on a water-bath, cool and dissolve the residue in 5 mL of *acetone R*. Add 0.2 mL of *alcoholic potassium hydroxide solution R*. A green colour is produced.

D. It gives reaction (a) of chlorides (*2.3.1*).

TESTS

Solution S. Dissolve 1.0 g in *carbon dioxide-free water R* and dilute to 20 mL with the same solvent.

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

pH (*2.2.3*): 4.0 to 5.5.

Dilute 1 mL of solution S to 10 mL with *carbon dioxide-free water R*.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 50.0 mg of the substance to be examined in the mobile phase and dilute to 10.0 mL with the mobile phase.

Reference solution (a). Dissolve 50.0 mg of *2,6-dimethylaniline R* (impurity A) in the mobile phase and dilute to 100.0 mL with the mobile phase. Dilute 10.0 mL of this solution to 100.0 mL with the mobile phase.

Reference solution (b). Dissolve 5 mg of *2-chloro-N-(2,6-dimethylphenyl)acetamide R* (impurity H) in the mobile phase and dilute to 10 mL with the mobile phase.

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

Reference solution (d). Mix 1.0 mL of reference solution (a), 1.0 mL of reference solution (b) and 1.0 mL of reference solution (c) and dilute to 100.0 mL with the mobile phase.

Column:

– *size*: *l* = 0.15 m, Ø = 3.9 mm;
– *stationary phase*: *end-capped polar-embedded octadecylsilyl amorphous organosilica polymer R* (5 µm);
– *temperature*: 30 °C.

Mobile phase: mix 30 volumes of *acetonitrile for chromatography R* and 70 volumes of a 4.85 g/L solution of *potassium dihydrogen phosphate R* adjusted to pH 8.0 with *strong sodium hydroxide solution R*.

Flow rate: 1.0 mL/min.

Detection: spectrophotometer at 230 nm.

Injection: 20 µL.

Run time: 3.5 times the retention time of lidocaine.

Relative retention with reference to lidocaine (retention time = about 17 min): impurity H = about 0.37; impurity A = about 0.40.

System suitability: reference solution (d):

– *resolution*: minimum 1.5 between the peaks due to impurities H and A.

Limits:

– *impurity A*: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (d) (0.01 per cent);
– *unspecified impurities*: for each impurity, not more than the area of the peak due to lidocaine in the chromatogram obtained with reference solution (d) (0.10 per cent);
– *total*: not more than 5 times the area of the peak due to lidocaine in the chromatogram obtained with reference solution (d) (0.5 per cent);
– *disregard limit*: 0.5 times the area of the peak due to lidocaine in the chromatogram obtained with reference solution (d) (0.05 per cent).

Heavy metals (*2.4.8*): maximum 5 ppm.

Dissolve 1.0 g in *water R* and dilute to 25 mL with the same solvent. Carry out the prefiltration. 10 mL of the prefiltrate complies with test E. Prepare the reference solution using 2 mL of *lead standard solution (1 ppm Pb) R*.

Water (*2.5.12*): 5.5 per cent to 7.0 per cent, determined on 0.25 g.

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

ASSAY

Dissolve 0.220 g in 50 mL of *ethanol (96 per cent) R* and add 5.0 mL of *0.01 M hydrochloric acid*. 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 27.08 mg of $C_{14}H_{23}ClN_2O$.

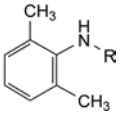
STORAGE

Protected from light.

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, H, I, J, K*.



A. R = H: 2,6-dimethylaniline,

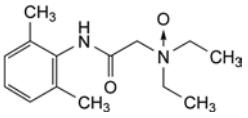
C. R = CO-CH_3: *N*-(2,6-dimethylphenyl)acetamide,

D. R = CO-CH_2-NH-C_2H_5: *N*-(2,6-dimethylphenyl)-2-(ethylamino)acetamide,

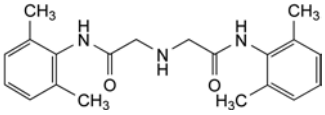
G. R = CO-CH_2-NH-$CH(CH_3)_2$: *N*-(2,6-dimethylphenyl)-2-[(1-methylethyl)amino]acetamide,

H. R = CO-CH_2-Cl: 2-chloro-*N*-(2,6-dimethylphenyl)acetamide,

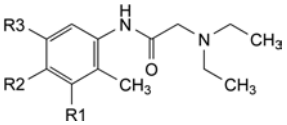
K. R=CO-CH_2-$N(CH_3)C_2H_5$: *N*-(2,6-dimethylphenyl)-2-(ethylmethylamino)acetamide,



B. 2-(diethylazinoyl)-*N*-(2,6-dimethylphenyl)acetamide (lidocaine N^2-oxide),



E. 2-2′-(azanediyl)bis[*N*-(2,6-dimethylphenyl)acetamide],



F. R1 = CH_3, R2 = R3 = H: 2-(diethylamino)-*N*-(2,3-dimethylphenyl)acetamide,

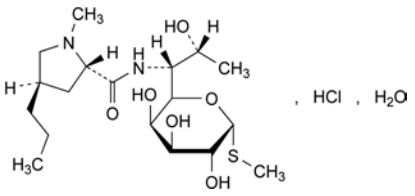
I. R1 = R3 = H, R2 = CH_3: 2-(diethylamino)-*N*-(2,4-dimethylphenyl)acetamide,

J. R1 = R2 = H, R3 = CH_3: 2-(diethylamino)-*N*-(2,5-dimethylphenyl)acetamide.

01/2008:0583

LINCOMYCIN HYDROCHLORIDE

Lincomycini hydrochloridum



$C_{18}H_{35}ClN_2O_6S,H_2O$ M_r 461.0

[7179-49-9]

DEFINITION

Lincomycin hydrochloride consists mainly of the methyl 6,8-dideoxy-6-[[[(2*S*,4*R*)-1-methyl-4-propylpyrrolidin-2-yl]carbonyl]amino]-1-thio-D-*erythro*-α-D-*galacto*-octopyranoside hydrochloride, an antimicrobial substance produced by *Streptomyces lincolnensis* var. *lincolnensis* or by any other means. It contains not less than 89.5 per cent and not more than 102.0 per cent of lincomycin hydrochloride ($C_{18}H_{35}ClN_2O_6S$), calculated with reference to the anhydrous substance.