– *stationary phase*: *octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase: *phosphoric acid R, acetonitrile R,* 10 g/l solution of *ammonium dihydrogen phosphate R* (0.1:45:55 *V/V/V*).

Flow rate: 1 ml/min.

Detection: spectrophotometer at 220 nm.

Injection: 100 µl.

System suitability: reference solution (c):

– *resolution*: minimum 2.2 between the peaks due to clemastine and impurity C.

Limit:

– *impurity C*: not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.3 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 for 6 h.

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

ASSAY

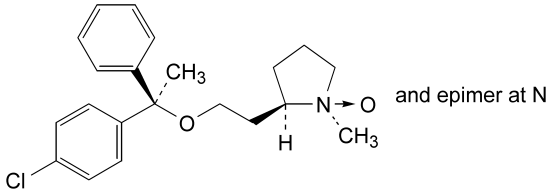
Dissolve 0.350 g in 60 ml of *anhydrous acetic acid R*. Titrate with *0.1 M perchloric acid,* determining the end-point potentiometrically (*2.2.20*).

1 ml of *0.1 M perchloric acid* is equivalent to 46.00 mg of $C_{25}H_{30}ClNO_5$.

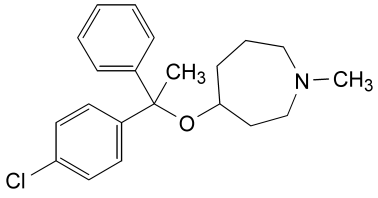
IMPURITIES

Specified impurities: A, B, C.

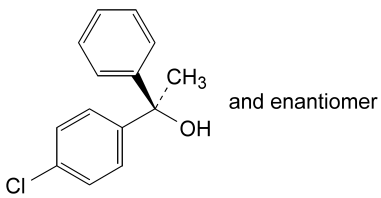
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph *Substances for pharmaceutical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



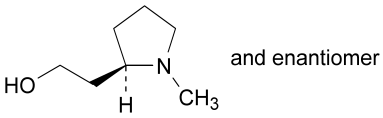
A. (1*RS*,2*R*)-2-[2-[(*R*)-1-(4-chlorophenyl)-1-phenylethoxy]-ethyl]-1-methylpyrrolidine 1-oxide,



B. 4-[1-(4-chlorophenyl)-1-phenylethoxy]-1-methylazepane,



C. (*RS*)-1-(4-chlorophenyl)-1-phenylethanol,

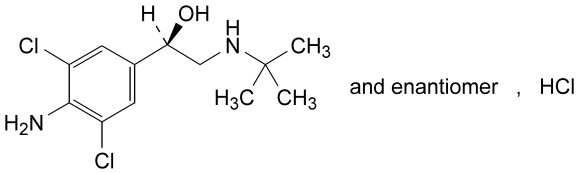


D. 2-[(2*RS*)-1-methylpyrrolidin-2-yl]ethanol.

01/2008:1409

CLENBUTEROL HYDROCHLORIDE

Clenbuteroli hydrochloridum



$C_{12}H_{19}Cl_3N_2O$ M_r 313.7
[21898-19-1]

DEFINITION

(1*RS*)-1-(4-Amino-3,5-dichlorophenyl)-2-[(1,1-dimethylethyl)amino]ethanol hydrochloride.

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

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: soluble in water and in ethanol (96 per cent), slightly soluble in acetone.

mp: about 173 °C, with decomposition.

IDENTIFICATION

First identification: A, C.

Second identification: B, C.

A. Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *clenbuterol hydrochloride CRS.*

B. Thin-layer chromatography (*2.2.27*).

Test solution. Dissolve 10 mg of the substance to be examined in 10 ml of *methanol R.*

Reference solution. Dissolve 10 mg of *clenbuterol hydrochloride CRS* in 10 ml of *methanol R.*

Plate: *TLC silica gel F_{254} plate R.*

Mobile phase: *ammonia R, anhydrous ethanol R, toluene R* (0.15:10:15 *V/V/V*).

Application: 10 µl.

Development: over a path of 10 cm.

Drying: in air.

Detection: spray with a 10 g/l solution of *sodium nitrite R* in *1 M hydrochloric acid* and dip after 10 min in a 4 g/l solution of *naphthylethylenediamine dihydrochloride R* in *methanol R*. Allow to dry in air.

Results: the principal spot in the chromatogram obtained with the test solution is similar in position, colour and size to the principal spot in the chromatogram obtained with the reference solution.

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

TESTS

Solution S. Dissolve 0.5 g in 10 ml of *carbon dioxide-free water R.*

Appearance of solution. Solution S is not more opalescent than reference suspension II (*2.2.1*) and not more intensely coloured than reference solution Y_6 (*2.2.2, Method II*).

pH (*2.2.3*): 5.0 to 7.0 for solution S.

Optical rotation (*2.2.7*): – 0.10° to + 0.10°.

Dissolve 0.30 g in *water R* and dilute to 10.0 ml with the same solvent. Filter if necessary.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Disperse 100.0 mg of the substance to be examined in the mobile phase and dilute to 50.0 ml with the mobile phase.

Reference solution (a). Dilute 0.1 ml of the test solution to 100.0 ml with *water R*.

Reference solution (b). Dissolve 5 mg of *clenbuterol impurity B CRS* in 10 ml of the mobile phase, add 2.5 ml of the test solution and dilute to 25.0 ml with the mobile phase.

Column:

– *size*: *l* = 0.125 m, Ø = 4 mm,
– *stationary phase*: *end-capped octadecylsilyl silica gel for chromatography R* (5 µm),
– *temperature*: 40 °C.

Mobile phase: mix 200 volumes of *acetonitrile R*, 200 volumes of *methanol R* and 600 volumes of a solution prepared as follows: dissolve 3.0 g of *sodium decanesulphonate R* and 5.0 g of *potassium dihydrogen phosphate R* in 900 ml of *water R*, adjust to pH 3.0 with *dilute phosphoric acid R* and dilute to 1000 ml with *water R*.

Flow rate: 0.5 ml/min.

Detection: spectrophotometer at 215 nm.

Injection: 5 µl.

Run time: 1.5 times the retention time of clenbuterol .

Retention time: clenbuterol = about 29 min.

System suitability: reference solution (b):

– *resolution*: minimum 4.0 between the peaks due to impurity B and clenbuterol.

Limits:

– *impurities A, B, C, D, E, F*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (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*: 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Water (*2.5.12*): maximum 1.0 per cent, determined on 0.500 g.

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

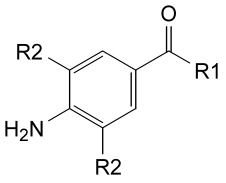
ASSAY

Dissolve 0.250 g in 50 ml of *ethanol (96 per cent) R* and add 5.0 ml of *0.01 M hydrochloric acid*. Titrate with *0.1 M sodium hydroxide*, determining the end-point potentiometrically (*2.2.20*). Read the volume added between the 2 points of inflexion.

1 ml of *0.1 M sodium hydroxide* is equivalent to 31.37 mg of $C_{12}H_{19}Cl_3N_2O$.

IMPURITIES

Specified impurities: A, B, C, D, E, F.



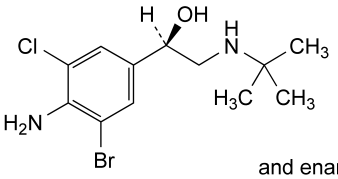
A. R1 = H, R2 = Cl: 4-amino-3,5-dichlorobenzaldehyde,

B. R1 = CH_2-NH-$C(CH_3)_3$, R2 = Cl: 1-(4-amino-3,5-dichlorophenyl)-2-[(1,1-dimethylethyl)amino]ethanone,

C. R1 = CH_3, R2 = Cl: 1-(4-amino-3,5-dichlorophenyl)ethanone,

D. R1 = CH_3, R2 = H: 1-(4-aminophenyl)ethanone,

E. R1 = CH_2Br, R2 = Cl: 1-(4-amino-3,5-dichlorophenyl)-2-bromoethanone,



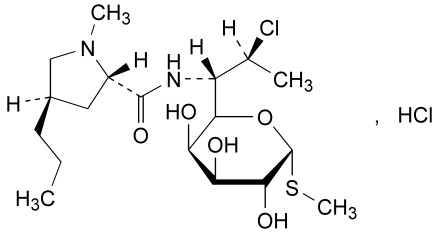
and enantiomer

F. (1*RS*)-1-(4-amino-3-bromo-5-chlorophenyl)-2-[(1,1-dimethylethyl)amino]ethanol.

01/2008:0582
corrected 6.0

CLINDAMYCIN HYDROCHLORIDE

Clindamycini hydrochloridum



, HCl

$C_{18}H_{34}Cl_2N_2O_5S$ M_r 461.5
[21462-39-5]

DEFINITION

Methyl 7-chloro-6,7,8-trideoxy-6-[[[(2*S*,4*R*)-1-methyl-4-propylpyrrolidin-2-yl]carbonyl]amino]-1-thio-L-*threo*-α-D-*galacto*-octopyranoside hydrochloride. It contains a variable quantity of water.

Semi-synthetic product derived from a fermentation product.

Content: 91.0 per cent to 102.0 per cent (anhydrous substance).

CHARACTERS

Appearance: white or almost white, crystalline powder.

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

IDENTIFICATION

First identification: A, D.

Second identification: B, C, D.

A. Infrared absorption spectrophotometry (*2.2.24*).
Comparison: *clindamycin hydrochloride CRS*.