Limits:

- *impurities A, B, C, D, E, F*: for each impurity, not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent),
- *unspecified impurities*: for each impurity, not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent),
- *total*: not more than 1.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.3 per cent),
- *disregard limit*: 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.02 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.

Sulphated ash (*2.4.14*): maximum 0.2 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.100 g in 70 ml of a mixture of 30 volumes of *water R* and 70 volumes of *acetone R*. Titrate with *0.1 M sodium hydroxide* to the second point of inflexion. Determine the end-point potentiometrically (*2.2.20*). Carry out a blank titration.

1 ml of *0.1 M sodium hydroxide* is equivalent to 15.39 mg of $C_{21}H_{27}Cl_3N_2O_3$.

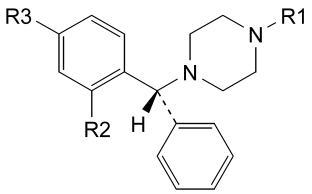
STORAGE

Protected from light.

IMPURITIES

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

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*): *G.*



and enantiomer

A. R1 = R2 = H, R3 = Cl: (*RS*)-1-[(4-chlorophenyl)phenylmethyl]piperazine,

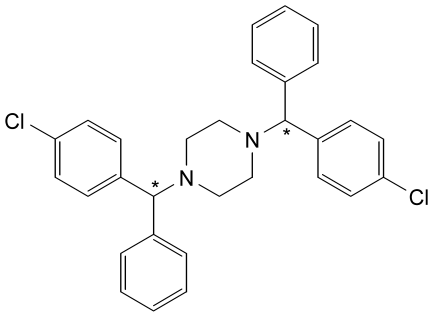
B. R1 = CH_2-CO_2H, R2 = H, R3 = Cl: (*RS*)-2-[4-[(4-chlorophenyl)phenylmethyl]piperazin-1-yl]acetic acid,

C. R1 = CH_2-CH_2-O-CH_2-CO_2H, R2 = Cl, R3 = H: (*RS*)-2-[2-[4-[(2-chlorophenyl)phenylmethyl]piperazin-1-yl]ethoxy]acetic acid,

E. R1 = CH_2-[CH_2-O-CH_2]$_2$-CO_2H, R2 = H, R3 = Cl: (*RS*)-2-[2-[2-[4-[(4-chlorophenyl)phenylmethyl]piperazin-1-yl]ethoxy]ethoxy]acetic acid (ethoxycetirizine),

F. R1 = CH_2-CH_2-O-CH_2-CO_2H, R2 = R3 = H: [2-[4-(diphenylmethyl)piperazin-1-yl]ethoxy]acetic acid,

G. R1 = CH_2-CH_2-OH, R2 = H, R3 = Cl: 2-[4-[(*RS*)-(4-chlorophenyl)phenylmethyl]piperazin-1-yl]ethanol,



D. 1,4-bis[(4-chlorophenyl)phenylmethyl]piperazine.

01/2008:0702

CETOSTEARYL ALCOHOL

Alcohol cetylicus et stearylicus

DEFINITION

Mixture of solid aliphatic alcohols, mainly octadecan-1-ol (stearyl alcohol; $C_{18}H_{38}O$; M_r 270.5) and hexadecan-1-ol (cetyl alcohol; $C_{16}H_{34}O$; M_r 242.4), of animal or vegetable origin.

Content:

- *stearyl alcohol*: minimum 40.0 per cent,
- *sum of the contents of stearyl alcohol and cetyl alcohol*: minimum 90.0 per cent.

CHARACTERS

Appearance: white or pale yellow, wax-like mass, plates, flakes or granules.

Solubility: practically insoluble in water, soluble in ethanol (96 per cent) and in light petroleum. When melted, it is miscible with fatty oils, with liquid paraffin and with melted wool fat.

IDENTIFICATION

Examine the chromatograms obtained in the assay.

Results: the 2 principal peaks in the chromatogram obtained with the test solution are similar in retention time to the principal peaks in the chromatogram obtained with the reference solution.

TESTS

Appearance of solution. The solution is clear (*2.2.1*) and not more intensely coloured than reference solution B_6 (*2.2.2, Method II*).

Dissolve 0.50 g in 20 ml of boiling *ethanol (96 per cent) R*. Allow to cool.

Melting point (*2.2.14*): 49 °C to 56 °C.

Acid value (*2.5.1*): maximum 1.0.

Hydroxyl value (*2.5.3, Method A*): 208 to 228.

Iodine value (*2.5.4, Method A*): maximum 2.0.

Dissolve 2.00 g in *methylene chloride R* and dilute to 25 ml with the same solvent.

Saponification value (*2.5.6*): maximum 2.0.

ASSAY

Gas chromatography (*2.2.28*): use the normalisation procedure.

Test solution. Dissolve 0.100 g of the substance to be examined in *ethanol (96 per cent) R* and dilute to 10.0 ml with the same solvent.

Reference solution. Dissolve 60 mg of *cetyl alcohol CRS* and 40 mg of *stearyl alcohol CRS* in *ethanol (96 per cent) R* and dilute to 10 ml with the same solvent. Dilute 1 ml of this solution to 10 ml with *ethanol (96 per cent) R*.

Column:

– *size*: *l* = 30 m, Ø = 0.32 mm,

– *stationary phase*: *poly(dimethyl)siloxane R* (1 µm).

Carrier gas: *helium for chromatography R*.

Flow rate: 1 ml/min.

Split ratio: 1:100.

Temperature:

	Time (min)	Temperature (°C)
Column	0 - 20	150 → 250
	20 - 40	250
Injection port		250
Detector		250

Detection: flame ionisation.

Injection: 1 µl.

System suitability: reference solution:

– *resolution*: minimum 5.0 between the peaks due to cetyl alcohol and stearyl alcohol.

Calculate the percentage contents of $C_{16}H_{34}O$ and $C_{18}H_{38}O$.

01/2008:0801
corrected 6.0

CETOSTEARYL ALCOHOL (TYPE A), EMULSIFYING

Alcohol cetylicus et stearylicus emulsificans A

DEFINITION

Mixture of cetostearyl alcohol and sodium cetostearyl sulphate. A suitable buffer may be added.

Content:

– *cetostearyl alcohol*: minimum 80.0 per cent (anhydrous substance),

– *sodium cetostearyl sulphate*: minimum 7.0 per cent (anhydrous substance).

CHARACTERS

Appearance: white or pale yellow, waxy mass, plates, flakes or granules.

Solubility: soluble in hot water giving an opalescent solution, practically insoluble in cold water, slightly soluble in ethanol (96 per cent).

IDENTIFICATION

First identification: B, C, D.

Second identification: A, C.

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

Test solution (a). Dissolve 0.1 g of the substance to be examined in 10 ml of *trimethylpentane R*, heating on a water-bath. Shake with 2 ml of *ethanol (70 per cent V/V) R* and allow to separate. Use the lower layer as test solution (b). Dilute 1 ml of the upper layer to 8 ml with *trimethylpentane R*.

Test solution (b). Use the lower layer obtained in the preparation of test solution (a).

Reference solution (a). Dissolve 40 mg of *cetostearyl alcohol R* in 10 ml of *trimethylpentane R*.

Reference solution (b). Dissolve 20 mg of *sodium cetostearyl sulphate R* in 10 ml of *ethanol (70 per cent V/V) R*, heating on a water-bath.

Plate: *TLC silanised silica gel plate R*.

Mobile phase: *water R, acetone R, methanol R* (20:40:40 *V/V/V*).

Application: 2 µl.

Development: over a path of 12 cm.

Drying: in air.

Detection: spray with a 50 g/l solution of *phosphomolybdic acid R* in *ethanol (96 per cent) R*. Heat at 120 °C until spots appear (about 3 h).

Results:

– the 2 principal spots in the chromatogram obtained with test solution (a) are similar in position and colour to the principal spots in the chromatogram obtained with reference solution (a),

– 2 of the spots in the chromatogram obtained with test solution (b) are similar in position and colour to the principal spots in the chromatogram obtained with reference solution (b).

B. Examine the chromatograms obtained in the assay.

Results: the 2 principal peaks in the chromatogram obtained with test solution (b) are similar in retention time to the 2 principal peaks in the chromatogram obtained with the reference solution.

C. It gives a yellow colour to a non-luminous flame.

D. To 0.3 g add 20 ml of *anhydrous ethanol R* and heat to boiling on a water-bath with shaking. Filter the mixture immediately, evaporate to dryness and take up the residue in 7 ml of *water R*. To 1 ml of the solution add 0.1 ml of a 1 g/l solution of *methylene blue R*, 2 ml of *dilute sulphuric acid R* and 2 ml of *methylene chloride R* and shake. A blue colour develops in the lower layer.

TESTS

Acid value (*2.5.1*): maximum 2.0.

Iodine value (*2.5.4, Method A*): maximum 3.0.

Dissolve 2.00 g in 25 ml of *methylene chloride R*.

Saponification value (*2.5.6*): maximum 2.0.

Water (*2.5.12*): maximum 3.0 per cent, determined on 2.50 g.

ASSAY

Cetostearyl alcohol. Gas chromatography (*2.2.28*).

Internal standard solution. Dissolve 0.60 g of *heptadecanol CRS* in *anhydrous ethanol R* and dilute to 150 ml with the same solvent.

Test solution (a). Dissolve 0.300 g of the substance to be examined in 50 ml of the internal standard solution, add 50 ml of *water R* and shake with 4 quantities, each of 25 ml, of *pentane R*, adding *sodium chloride R*, if necessary, to facilitate the separation of the layers. Combine the organic layers. Wash with 2 quantities, each of 30 ml, of *water R*, dry over *anhydrous sodium sulphate R* and filter.

Test solution (b). Dissolve 0.300 g of the substance to be examined in 50 ml of *anhydrous ethanol R*, add 50 ml of *water R* and shake with 4 quantities, each of 25 ml, of *pentane R*, adding *sodium chloride R*, if necessary, to facilitate the separation of the layers. Combine the organic layers. Wash with 2 quantities, each of 30 ml, of *water R*, dry over *anhydrous sodium sulphate R* and filter.