Relative retention with reference to carboprost (retention time = about 80 min): impurity B = about 0.85; impurity A = about 0.9.

Identification of impurities: use the chromatogram obtained with reference solution (a) and the chromatogram supplied with *carboprost trometamol CRS* to identify the peak due to impurity A.

System suitability:

- *resolution*: minimum 3.4 between the peaks due to impurity B and carboprost in the chromatogram obtained with reference solution (b);
- *peak-to-valley ratio*: minimum 3.0, where H_p = height above the baseline of the peak due to impurity A and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to impurity B in the chromatogram obtained with reference solution (a).

Limits:

- *impurity A*: not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (c) (3.0 per cent),
- *impurity B*: not more than the area of the principal peak in the chromatogram obtained with reference solution (c) (1.0 per cent),
- *unspecified impurities*: for each impurity, not more than 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.10 per cent),
- *total*: not more than 4 times the area of the principal peak in the chromatogram obtained with reference solution (c) (4.0 per cent),
- *disregard limit*: 0.05 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.05 per cent).

Water (*2.5.32*): maximum 0.5 per cent, determined on 50 mg.

ASSAY

Liquid chromatography (*2.2.29*) as described in the test for related substances with the following modifications.

Mobile phase: mix 27 volumes of *acetonitrile R1* and 73 volumes of a 2.44 g/L solution of *sodium dihydrogen phosphate R* in *water for chromatography R* previously adjusted to pH 2.5 with *phosphoric acid R*.

Injection: test solution and reference solution (a).

Run time: 1.2 times the retention time of carboprost.

Retention time: carboprost = about 29 min.

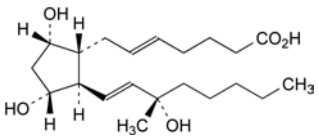
Calculate the percentage content of $C_{25}H_{47}NO_8$ using the declared content of *carboprost trometamol CRS*.

STORAGE

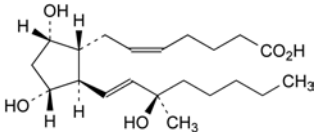
At a temperature below – 15 ° C.

IMPURITIES

Specified impurities: A, B.



A. (5*E*)-7-[(1*R*,2*R*,3*R*,5*S*)-3,5-dihydroxy-2-[(1*E*,3*S*)-3-hydroxy-3-methyloct-1-enyl]cyclopentyl]hept-5-enoic acid,

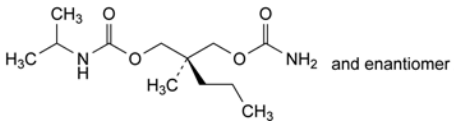


B. (5*Z*)-7-[(1*R*,2*R*,3*R*,5*S*)-3,5-dihydroxy-2-[(1*E*,3*R*)-3-hydroxy-3-methyloct-1-enyl]cyclopentyl]hept-5-enoic acid.

01/2008:1689

CARISOPRODOL

Carisoprodolum



$C_{12}H_{24}N_2O_4$ M_r 260.3
[78-44-4]

DEFINITION

(2*RS*)-2-[(Carbamoyloxy)methyl]-2-methylpentyl (1-methylethyl)carbamate.

Content: 98.0 per cent to 102.0 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, fine powder.

Solubility: very slightly soluble in water, freely soluble in acetone, in alcohol and in methylene chloride.

IDENTIFICATION

First identification: A, B.

Second identification: A, C, D.

A. Melting point (*2.2.14*): 92 °C to 95 °C.

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

C. Examine the chromatograms obtained in the test for related substances.
Results: the principal spot in the chromatogram obtained with test solution (b) is similar in position, colour and size to the principal spot in the chromatogram obtained with reference solution (d).

D. Dissolve 0.2 g in 15 mL of a 28 g/L solution of *potassium hydroxide R* in *alcohol R* and boil under a reflux condenser for 15 min. Add 0.5 mL of *glacial acetic acid R* and 1 mL of a 50 g/L solution of *cobalt nitrate R* in *ethanol R*. An intense blue colour develops.

TESTS

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

Dissolve 2.5 g in *alcohol R* and dilute to 25.0 mL with the same solvent.

Related substances. Thin-layer chromatography (*2.2.27*).

Test solution (a). Dissolve 0.20 g of the substance to be examined in *methylene chloride R* and dilute to 10 mL with the same solvent.

Test solution (b). Dilute 1 mL of test solution (a) to 10 mL with *methylene chloride R*.

Reference solution (a). Dissolve 5.0 mg of *meprobamate CRS* in *methylene chloride R* and dilute to 50 mL with the same solvent.

Reference solution (b). Dilute 1 mL of test solution (b) to 50 mL with *methylene chloride R*.

Reference solution (c). Dilute 5 mL of reference solution (b) to 10 mL with *methylene chloride R*.

Reference solution (d). Dissolve 20 mg of *carisoprodol CRS* in *methylene chloride R* and dilute to 10 mL with the same solvent.

Reference solution (e). Dissolve 10 mg of *carisoprodol impurity A CRS* in 5 mL of reference solution (d) and dilute to 50 mL with *methylene chloride R*.

Plate: *TLC silica gel plate R*.

Mobile phase: *acetone R, methylene chloride R* (20:80 *V/V*).

Application: 5 µL.

Development: over a path of 15 cm.

Drying: in air for 15 min.

Detection: spray with a solution prepared as follows: dissolve 5 g of *phosphomolybdic acid R* in a mixture of 50 mL of *glacial acetic acid R* and 10 mL of *sulfuric acid R*, and dilute to 100 mL with *glacial acetic acid R*. Heat the plate at 100-105 °C for 30 min.

System suitability:

- the chromatogram obtained with reference solution (c) shows 1 clearly visible spot,
- the chromatogram obtained with reference solution (e) shows 2 clearly separated spots.

Limits: in the chromatogram obtained with test solution (a):

- *impurity D*: any spot due to impurity D is not more intense than the spot in the chromatogram obtained with reference solution (a) (0.5 per cent),
- *any other impurity*: any spot, apart from the principal spot and any spot due to impurity D, is not more intense than the spot in the chromatogram obtained with reference solution (b) (0.2 per cent).

Heavy metals (*2.4.8*): maximum 10 ppm.

2.0 g complies with limit test C. Prepare the standard using 2 mL of *lead standard solution (10 ppm Pb) R*.

Loss on drying (*2.2.32*): maximum 0.5 per cent, determined on 1.000 g *in vacuo* at 60 °C for 3 h.

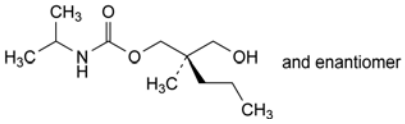
Sulfated ash (*2.4.14*): maximum 0.1 per cent, determined on 1.0 g.

ASSAY

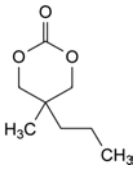
Dissolve 0.100 g in 15 mL of a 25 per cent *V/V* solution of *sulfuric acid R* and boil under a reflux condenser for 3 h. Cool, dissolve by cautiously adding 30 mL of *water R*, cool again and place in a steam-distillation apparatus. Add 40 mL of *strong sodium hydroxide solution R* and distil immediately by passing steam through the mixture. Collect the distillate into 40 mL of a 40 g/L solution of *boric acid R* until the total volume in the receiver reaches about 200 mL. Add 0.25 mL of *methyl red mixed solution R*. Titrate with *0.1 M hydrochloric acid*, until the colour changes from green to violet. Carry out a blank titration.

1 mL of *0.1 M hydrochloric acid* is equivalent to 13.02 mg of $C_{12}H_{24}N_2O_4$.

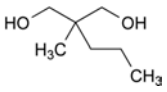
IMPURITIES



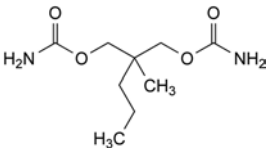
A. (2*RS*)-2-(hydroxymethyl)-2-methylpentyl (1-methylethyl)-carbamate,



B. 5-methyl-5-propyl-1,3-dioxan-2-one,



C. 2-methyl-2-propylpropane-1,3-diol,



D. 2-methyl-2-propylpropane-1,3-diyl dicarbamate (meprobamate).

04/2010:2360
corrected 7.0

CARMELLOSE

Carmellosum

DEFINITION

Polycarboxymethylether of cellulose.

CHARACTERS

Appearance: white or almost white powder, hygroscopic.

Solubility: practically insoluble in anhydrous ethanol. It swells with water to form a suspension and becomes viscid in 1 M sodium hydroxide.

IDENTIFICATION

A. pH (*2.2.3*): 3.5 to 5.0.
Suspend 1.0 g in 100 mL of *water R*.

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

TESTS

Chlorides: maximum 0.36 per cent.

Shake 0.8 g with 50 mL of *water R*, dissolve in 10 mL of *1 M sodium hydroxide* and dilute to 100 mL with *water R*. Heat on a water-bath a mixture of 10 mL of *dilute nitric acid R* and 20 mL of this solution until a flocculent precipitate is produced. Cool, centrifuge and take out the supernatant liquid. Wash the precipitate with 3 quantities, each of 10 mL, of *water R*, centrifuging each time. Combine the supernatant liquid and the washings and dilute to 100 mL with *water R*. To 25 mL of this solution add 6 mL of *dilute nitric acid R* and dilute to 50 mL with *water R* (test solution). Prepare the reference solution with 0.40 mL of *0.01 M hydrochloric acid*. Add 1 mL of *silver nitrate solution R2* to the test solution and the reference solution. Allow to stand protected from light for 5 min. Any opalescence in the test solution is not more intense than that in the reference solution.

Sulfates: maximum 0.72 per cent.

Shake 0.40 g with 25 mL of *water R*, dissolve in 5 mL of *1 M sodium hydroxide* and add 20 mL of *water R*. Heat this solution with 2.5 mL of *hydrochloric acid R* in a water-bath until a flocculent precipitate is produced. Cool, centrifuge, and take out the supernatant liquid. Wash the precipitate with 3 quantities, each of 10 mL, of *water R*, centrifuging each time. Combine the supernatant liquid and the washings, and dilute to 100 mL with *water R*. Filter, and discard the first 5 mL of the filtrate. To 25 mL of the filtrate add 1 mL of *dilute hydrochloric acid R* and dilute to 50 mL with *water R* (test solution). Prepare the reference solution with 1.5 mL of *0.005 M sulfuric acid*. Add 2 mL of a 120 g/L solution of *barium chloride R* to the test solution and the reference solution. Mix and allow to stand for 10 min. The white turbidity produced in the test solution is not thicker than that in the reference solution.

Heavy metals: maximum 20 ppm.

Place 1.0 g in a quartz or porcelain crucible. Cover loosely with a lid and carbonise by gentle ignition. Cool and add 2 mL of *nitric acid R* and 5 drops of *sulfuric acid R*. Heat cautiously until white fumes are no longer evolved and incinerate by ignition at 500-600 °C. Cool and add 2 mL of *hydrochloric acid R*. Evaporate to dryness on a water-bath. Moisten the