– as mobile phase at a flow rate of 1 ml/min a mixture of 1 volume of *acetonitrile R*, 1 volume of *methanol R* and 2 volumes of a mixture prepared as follows: dissolve 2.0 g of *sodium octanesulphonate R* in *water R*, add 1.0 ml of *anhydrous acetic acid R* and dilute to 1000 ml with *water R*,
– as detector a spectrophotometer set at 280 nm,

maintaining the temperature of the column at 40 °C.

Inject 20 µl of the reference solution. When the chromatogram is recorded in the prescribed conditions, the retention time of pergolide is about 9 min. Adjust the sensitivity of the system so that the height of the principal peak in the chromatogram obtained with the reference solution is at least 50 per cent of the full scale of the recorder.

The assay is not valid unless the symmetry factor of the peak due to pergolide is at most 1.5.

Inject 20 µl of the test solution.

Calculate the percentage content of $C_{20}H_{30}N_2O_3S_2$ from the areas of the peaks and the declared content of *pergolide mesilate CRS*.

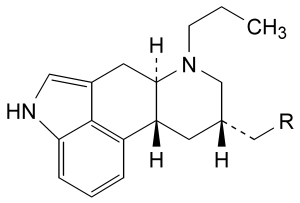
STORAGE

Store protected from light.

IMPURITIES

Specified impurities: A.

Other detectable impurities: B.



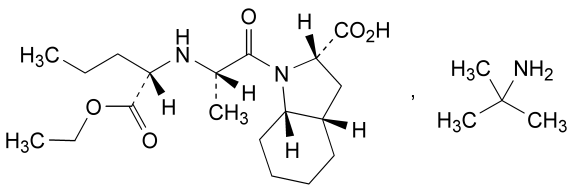
A. R = SO-CH_3: (6a*R*,9*R*,10a*R*)-9-[(methylsulphinyl)methyl]-7-propyl-4,6,6a,7,8,9,10,10a-octahydroindolo[4,3-*fg*]quinoline (pergolide sulphoxide),

B. R = SO_2-CH_3: (6a*R*,9*R*,10a*R*)-9-[(methylsulphonyl)methyl]-7-propyl-4,6,6a,7,8,9,10,10a-octahydroindolo[4,3-*fg*]quinoline (pergolide sulphone).

01/2005:2019

PERINDOPRIL *tert*-BUTYLAMINE

tert-Butylamini perindoprilum



$C_{23}H_{43}N_3O_5$ M_r 441.6

DEFINITION

2-Methylpropan-2-amine (2*S*,3a*S*,7a*S*)-1-[(2*S*)-2-[[(1*S*)-1-(ethoxycarbonyl)butyl]amino]propanoyl]octahydro-1*H*-indole-2-carboxylate.

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

CHARACTERS

Appearance: white or almost white, crystalline powder, slightly hygroscopic.

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

It shows polymorphism.

IDENTIFICATION

A. Specific optical rotation (*2.2.7*): −66 to −69 (anhydrous substance).

Dissolve 0.250 g in *alcohol R* and dilute to 25.0 ml with the same solvent.

B. Infrared absorption spectrophotometry (*2.2.24*).

Preparation: discs.

Comparison: *perindopril tert-butylamine CRS*.

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

C. Examine the chromatograms obtained in the test for impurity A.

Results: in the chromatogram obtained with the test solution a spot is observed with the same R_f as the spot with the higher R_f in the chromatogram with reference solution (c) (*tert*-butylamine).

TESTS

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

Test solution. Dissolve 0.20 g of the substance to be examined in *methanol R* and dilute to 10 ml with the same solvent.

Reference solution (a). Dissolve 5 mg of *perindopril impurity A CRS* in *methanol R* and dilute to 25.0 ml with the same solvent.

Reference solution (b). Dilute 5 ml of reference solution (a) to 20 ml with *methanol R*.

Reference solution (c). To 5 ml of reference solution (a) add 5 ml of a 20 g/l solution of *1,1-dimethylethylamine R* in *methanol R*.

Plate: *TLC silica gel plate R*.

Mobile phase: *glacial acetic acid R, toluene R, methanol R* (1:40:60 *V/V/V*).

Application: 10 µl; apply the test solution and reference solutions (b) and (c).

Development: in a saturated tank, over 2/3 of the plate.

Drying: in a current of warm air.

Detection: expose to iodine vapour for at least 20 h.

System suitability: the chromatogram obtained with reference solution (c) shows 2 clearly separated spots.

Limit:

– *impurity A*: any spot due to impurity A is not more intense than the spot in the chromatogram obtained with reference solution (b) (0.25 per cent).

Stereochemical purity. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 20 mg of the substance to be examined in *alcohol R* and dilute to 10.0 ml with the same solvent.

Reference solution (a). Dilute 1.0 ml of the test solution to 200.0 ml with *alcohol R*.

Reference solution (b). Dissolve 10 mg of *perindopril for stereochemical purity CRS* in *alcohol R* and dilute to 5.0 ml with the same solvent.

Reference solution (c). Dilute 10.0 ml of reference solution (a) to 50.0 ml with *alcohol R*.

Column:

– *size*: *l* = 0.25 m, Ø = 4.6 mm,

– *stationary phase*: spherical *octadecylsilyl silica gel for chromatography R* (5 µm) with a specific surface area of 450 m^2/g and a pore size of 10 nm,

– *temperature*: 50 °C for the column and at least 30 cm of the tubing preceding the column.

Mobile phase: mix, in the following order, 21.7 volumes of *acetonitrile R*, 0.3 volumes of *pentanol R* and 78 volumes of a 1.50 g/l solution of *sodium heptanesulphonate R*, previously adjusted to pH 2.0 with a mixture of equal volumes of *perchloric acid R* and *water R*.

Flow rate: 0.8 ml/min.

Detection: spectrophotometer at 215 nm.

Equilibration: minimum 4 h.

Injection: 10 µl.

Run time: 1.5 times the retention time of perindopril.

Retention time: perindopril = about 100 min.

System suitability:

– *signal-to-noise ratio*: minimum 3 for the principal peak in the chromatogram obtained with reference solution (c),

– *peak-to-valley ratio*: minimum 3, where H_p = height above the baseline of the peak due to impurity I and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to perindopril in the chromatogram obtained with reference solution (b),

– the chromatogram obtained with reference solution (b) is similar to the chromatogram provided with *perindopril for stereochemical purity CRS*.

Limits:

– *any impurity*: not more than 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent); disregard any peak with a retention time less than 0.6 times the retention time of perindopril and any peak with a retention time greater than 1.4 times the retention time of perindopril.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 60 mg of the substance to be examined in mobile phase A and dilute to 20.0 ml with mobile phase A.

Reference solution (a). Dissolve 15 mg of *perindopril for system suitability CRS* in mobile phase A and dilute to 5.0 ml with mobile phase A.

Reference solution (b). Dilute 1.0 ml of the test solution to 200.0 ml with mobile phase A.

Column:

– *size*: *l* = 0.25 m, Ø = 4 mm,

– *stationary phase*: spherical *octylsilyl silica gel for chromatography R* (4 µm) with a pore size of 6 nm,

– *temperature*: 70 °C.

Mobile phase:

– *mobile phase A*: dissolve 0.92 g of *sodium heptanesulphonate R* in 1000 ml of *water R*, add 1 ml of *triethylamine R* and adjust to pH 2.0 with a mixture of equal volumes of *perchloric acid R* and *water R*,

– *mobile phase B*: *acetonitrile R1*,

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 1	70	30
1 - 20	70 → 40	30 → 60
20 - 25	40	60
25 - 35	40 → 20	60 → 80
35 - 40	20 → 0	80 → 100
40 - 45	0 → 70	100 → 30

Flow rate: 1.5 ml/min.

Detection: spectrophotometer at 215 nm.

Injection: 20 µl.

Relative retention with reference to perindopril (retention time = about 8 min): impurity B = about 0.4; impurity C = about 0.8; impurity D = about 0.9; impurity E = about 1.4; impurity F = about 1.7; impurity G = about 2.2 and 2.3; impurity H = about 3.6 and 3.7.

System suitability: reference solution (a):

– *peak-to-valley ratio*: minimum 10, where H_p = height above the baseline of the peak due to impurity D and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to perindopril.

Limits:

– *impurity B*: not more than 0.6 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.3 per cent),

– *impurity E*: not more than 0.8 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.4 per cent),

– *impurities F, H*: for each impurity, not more than 0.4 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent),

– *any other impurity*: not more than 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent),

– *total*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (1 per cent),

– *disregard limit*: 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent).

Water (*2.5.12*): maximum 1.0 per cent, determined on 0.50 g.

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

ASSAY

Dissolve 0.160 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 22.08 mg of $C_{23}H_{43}N_3O_5$.

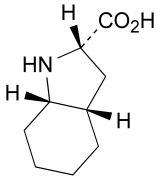
STORAGE

In an airtight container.

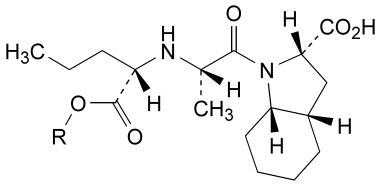
IMPURITIES

Specified impurities: A, B, E, F, H, I.

Other detectable impurities: C, D, G.

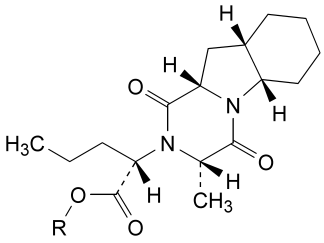


A. (2*S*,3a*S*,7a*S*)-octahydro-1*H*-indole-2-carboxylic acid,



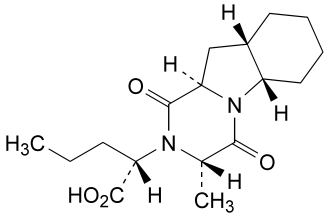
B. R = H: (2*S*,3a*S*,7a*S*)-1-[(2*S*)-2-[[(1*S*)-1-carboxybutyl]amino]propanoyl]octahydro-1*H*-indole-2-carboxylic acid,

E. R = $CH(CH_3)_2$: (2*S*,3a*S*,7a*S*)-1-[(2*S*)-2-[[(1*S*)-1-[(1-methylethoxy)carbonyl]butyl]amino]propanoyl]octahydro-1*H*-indole-2-carboxylic acid,

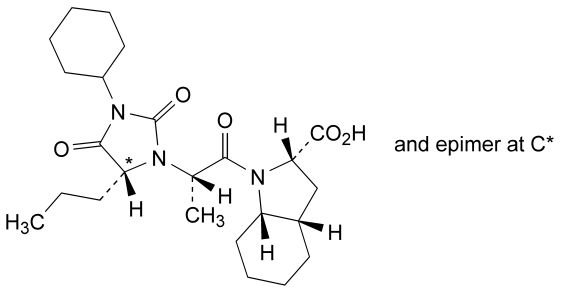


C. R = H: (2*S*)-2-[(3*S*,5a*S*,9a*S*,10a*S*)-3-methyl-1,4-dioxodecahydropyrazino[1,2-*a*]indol-2(1*H*)-yl]pentanoic acid,

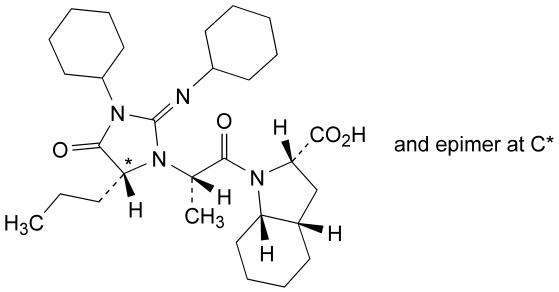
F. R = C_2H_5: ethyl (2*S*)-2-[(3*S*,5a*S*,9a*S*,10a*S*)-3-methyl-1,4-dioxodecahydropyrazino[1,2-*a*]indol-2(1*H*)-yl]pentanoate,



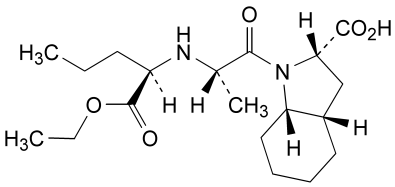
D. (2*S*)-2-[(3*S*,5aS,9a*S*,10a*R*)-3-methyl-1,4-dioxodecahydropyrazino[1,2-*a*]indol-2(1*H*)-yl]pentanoic acid,



G. (2*S*,3a*S*,7a*S*)-1-[(2*S*)-2-[(5*RS*)-3-cyclohexyl-2,4-dioxo-5-propylimidazolidin-1-yl]propanoyl]octahydro-1*H*-indole-2-carboxylic acid,



H. (2*S*,3a*S*,7a*S*)-1-[(2*S*)-2-[(5*RS*)-3-cyclohexyl-2-(cyclohexylimino)-4-oxo-5-propylimidazolidin-1-yl]propanoyl]octahydro-1*H*-indole-2-carboxylic acid,



I. (2*S*,3a*S*,7a*S*)-1-[(2*S*)-2-[[(1*R*)-1-(ethoxycarbonyl)butyl]amino]propanoyl]octahydro-1*H*-indole-2-carboxylic acid.

01/2005:0862

PERITONEAL DIALYSIS, SOLUTIONS FOR

Solutiones ad peritonealem dialysim

DEFINITION

Solutions for peritoneal dialysis are preparations for intraperitoneal use containing electrolytes with a concentration close to the electrolytic composition of plasma. They contain glucose in varying concentrations or other suitable osmotic agents.

Solutions for peritoneal dialysis are supplied in:

- rigid or semi-rigid plastic containers,
- flexible plastic containers fitted with a special connecting device; these are generally filled to a volume below their nominal capacity and presented in closed protective envelopes,
- glass containers.

The containers and closures comply with the requirements for containers for preparations for parenteral use (*3.2.1* and *3.2.2*).

Several formulations are used. The concentrations of the components per litre of solution are usually in the following range:

Table 0862.-1

	Expression in mmol	Expression in mEq
Sodium	125 - 150	125 - 150
Potassium	0 - 4.5	0 - 4.5
Calcium	0 - 2.5	0 - 5.0
Magnesium	0.25 - 1.5	0.50 - 3.0
Acetate and/or lactate and/or hydrogen carbonate	30 - 60	30 - 60
Chloride	90 - 120	90 - 120
Glucose	25 - 250	