– *total*: not more than 4 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.8 per cent);

– *disregard limit*: 0.25 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent).

Water (*2.5.12*): 7.5 per cent to 11.0 per cent, determined on 0.200 g.

Sulphated ash (*2.4.14*): maximum 0.2 per cent, determined on 0.50 g.

ASSAY

Dissolve 0.300 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 ethanolic sodium hydroxide*. Read the volume added between the 2 points of inflexion.

1 ml of *0.1 M ethanolic sodium hydroxide* is equivalent to 36.38 mg of $C_{19}H_{22}ClNO_4$.

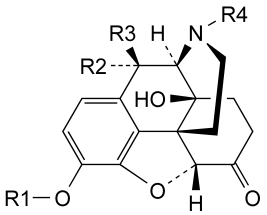
STORAGE

In an airtight container, 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*.



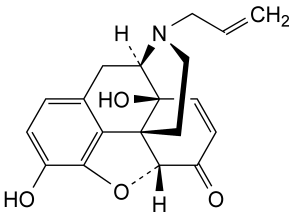
A. R1 = R2 = R3 = R4 = H: 4,5α-epoxy-3,14-dihydroxymorphinan-6-one (noroxymorphone),

B. R1 = R4 = CH_2-CH=CH_2, R2 = R3 = H: 4,5α-epoxy-14-hydroxy-17-(prop-2-enyl)-3-(prop-2-enyloxy)morphinan-6-one (3-*O*-allylnaloxone),

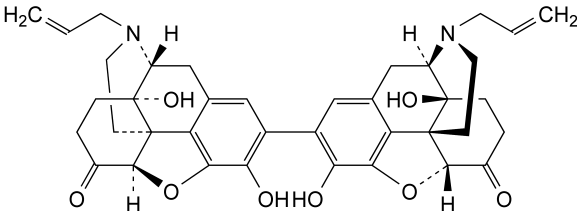
C. R1 = R3 = H, R2 = OH, R4 = CH_2-CH=CH_2: 4,5α-epoxy-3,10α,14-trihydroxy-17-(prop-2-enyl)morphinan-6-one (10α-hydroxynaloxone),

F. R1 = R2 = H, R3 = OH, R4 = CH_2-CH=CH_2: 4,5α-epoxy-3,10β,14-trihydroxy-17-(prop-2-enyl)morphinan-6-one (10β-hydroxynaloxone),

G. R1 = CH_3, R2 = R3 = H, R4 = CH_2-CH=CH_2: 4,5α-epoxy-14-hydroxy-3-methoxy-17-(prop-2-enyl)morphinan-6-one (3-*O*-methylnaloxone),



D. 7,8-didehydro-4,5α-epoxy-3,14-dihydroxy-17-(prop-2-enyl)morphinan-6-one (7,8-didehydronaloxone),

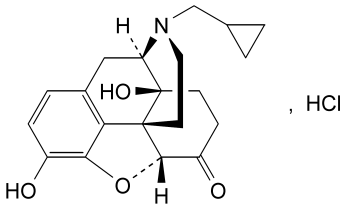


E. 4,5α:4′,5′α-diepoxy-3,3′,14,14′-tetrahydroxy-17,17′-bis(prop-2-enyl)-2,2′-bimorphinanyl-6,6′-dione (2,2′-binaloxone).

01/2008:1790

NALTREXONE HYDROCHLORIDE

Naltrexoni hydrochloridum



$C_{20}H_{24}ClNO_4$ M_r 377.9

DEFINITION

17-(Cyclopropylmethyl)-4,5α-epoxy-3,14-dihydroxymorphinan-6-one hydrochloride. It may be anhydrous, a monohydrate or a dihydrate, a mixture or a solvate.

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

CHARACTERS

Appearance: white or almost white powder, very hygroscopic.

Solubility: freely soluble in water, slightly soluble in ethanol (96 per cent), practically insoluble in methylene chloride.

IDENTIFICATION

A. Infrared absorption spectrophotometry (*2.2.24*).

Dissolve 20 mg in *water R* and dilute to 5 ml with the same solvent. Make alkaline with *dilute ammonia R1*. Shake with 10 ml of *methylene chloride R*, separate the organic layer and evaporate the solvent. Dry the residue obtained *in vacuo*.

Comparison: *naltrexone hydrochloride CRS*.

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

TESTS

Solution S. Dissolve 0.40 g in *carbon dioxide-free water R* and dilute to 20.0 ml with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution Y_6 or B_6 (*2.2.2, Method II*).

Acidity and alkalinity. To 10 ml of solution S, add 0.05 ml of *methyl red solution R*. Not more than 0.2 ml of *0.02 M sodium hydroxide* or *0.02 M hydrochloric acid* is required to change the colour of the indicator.

Specific optical rotation (*2.2.7*): – 187 to – 195 (anhydrous substance).

Dissolve 0.40 g in *water R* and dilute to 20.0 ml with the same solvent.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 20.0 mg of the substance to be examined in *0.1 M hydrochloric acid* and dilute to 10.0 ml with the same solvent.

Reference solution (a). Dissolve 5.0 mg of *naltrexone impurity C CRS* in *0.1 M hydrochloric acid* and dilute to 2.5 ml with the same solvent.

Reference solution (b). Dilute 1.0 ml of the test solution and 1.0 ml of reference solution (a) to 100.0 ml with *0.1 M hydrochloric acid*. Dilute 1.0 ml of this solution to 10.0 ml with *0.1 M hydrochloric acid*.

Column:

– *size*: *l* = 0.15 m, Ø = 4.6 mm,

– *stationary phase*: *octadecylsilyl silica gel for chromatography R1* (5 µm),

– *temperature*: 40 °C.

Mobile phase:

– *mobile phase A*: 1.1 g/l solution of *sodium octanesulphonate R* adjusted to pH 2.3 with *phosphoric acid R*;

– *mobile phase B*: *acetonitrile R*;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 45	90 → 55	10 → 45
45 - 47	55 → 90	45 → 10
47 - 55	90	10

Flow rate: 1.2 ml/min.

Detection: spectrophotometer at 230 nm.

Equilibration: 8 min.

Injection: 10 µl.

Relative retention with reference to naltrexone (retention time = about 16 min): impurity A = about 0.4; impurity B = about 0.7; impurity F = about 0.8; impurity G = about 0.9; impurity C = about 1.05; impurity H = about 1.1; impurity I = about 1.2; impurity J = about 1.3; impurity D = about 1.4; impurity E = 1.7.

System suitability: reference solution (b):

– *resolution*: minimum 2.0 between the peaks due to naltrexone and impurity C.

Limits:

– *correction factor*: for the calculation of content, multiply the peak area of impurity D by 0.4;

– *impurities C, D, E, F, G*: for each impurity, not more than twice the area of the peak due to naltrexone in the chromatogram obtained with reference solution (b) (0.2 per cent);

– *impurities A, B, H, I, J*: for each impurity, not more than the area of the peak due to naltrexone in the chromatogram obtained with reference solution (b) (0.1 per cent);

– *any other impurity*: for each impurity, not more than the area of the peak due to naltrexone in the chromatogram obtained with reference solution (b) (0.1 per cent);

– *total*: not more than 10 times the area of the peak due to naltrexone in the chromatogram obtained with reference solution (b) (1.0 per cent);

– *disregard limit*: 0.5 times the area of the peak due to naltrexone in the chromatogram obtained with reference solution (b) (0.05 per cent).

Ethanol (*2.4.24, System A*): maximum 3.0 per cent.

Test solution. Dissolve 0.25 g of the substance to be examined in *water R* and dilute to 10.0 ml with the same solvent.

Reference solution. Dilute 0.750 g of *anhydrous ethanol R* to 1000.0 ml with *water R*.

Water (*2.5.12*): maximum 10.0 per cent, determined on 0.200 g.

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

ASSAY

Dissolve 0.200 g in 60 ml of *ethanol (96 per cent) R*, add 1.0 ml of *0.1 M hydrochloric acid*. Carry out a potentiometric titration (*2.2.20*), using *0.1 M sodium hydroxide*. The curve shows 3 points of inflexion. Read the volume added between the first 2 points of inflexion.

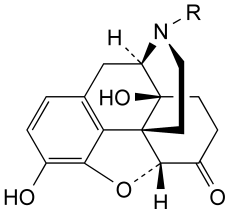
1 ml of *0.1 M sodium hydroxide* is equivalent to 37.79 mg of $C_{20}H_{24}ClNO_4$.

STORAGE

In an airtight container. Protected from light.

IMPURITIES

Specified impurities: A, B, C, D, E, F, G, H, I, J.

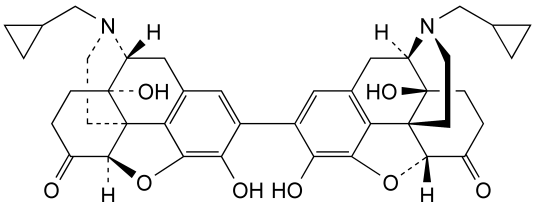


A. R = CHO: 17-formyl-4,5α-epoxy-3,14-dihydroxymorphinan-6-one,

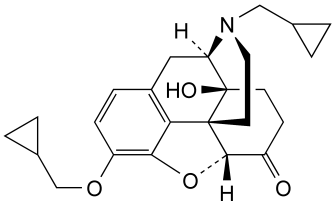
B. R = H: 4,5α-epoxy-3,14-dihydroxymorphinan-6-one (noroxymorphone),

C. R = CH_2-CH_2-CH=CH_2: 17-but-3-enyl-4,5α-epoxy-3,14-dihydroxymorphinan-6-one,

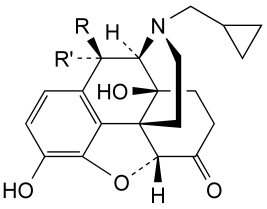
H. R = CH_2-CH_2-CH_2-CH_3: 17-butyl-4,5α-epoxy-3,14-dihydroxymorphinan-6-one,



D. 17,17′-bis(cyclopropylmethyl)-4,5α:4′,5′α-diepoxy-3,3′,14,14′-tetrahydroxy-2,2′-bimorphinanyl-6,6′-dione (pseudonaltrexone),



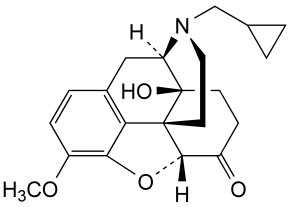
E. 3-(cyclopropylmethoxy)-17-(cyclopropylmethyl)-4,5α-epoxy-14-hydroxymorphinan-6-one,



F. R = H, R′ = OH: 17-(cyclopropylmethyl)-4,5α-epoxy-3,10α,14-trihydroxymorphinan-6-one,

G. R = OH, R′ = H: 17-(cyclopropylmethyl)-4,5α-epoxy-3,10β,14-trihydroxymorphinan-6-one,

I. R + R′ = O: 17-(cyclopropylmethyl)-4,5α-epoxy-3,14-dihydroxymorphinan-6,10-dione,

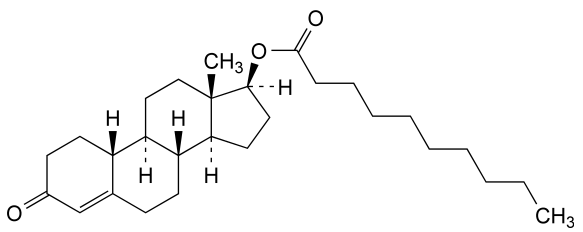


J. 17-(cyclopropylmethyl)-4,5α-epoxy-14-hydroxy-3-methoxymorphinan-6-one.

01/2008:1992

NANDROLONE DECANOATE

Nandroloni decanoas



$C_{28}H_{44}O_3$ M_r 428.7
[360-70-3]

DEFINITION

3-Oxoestr-4-en-17β-yl decanoate.

Content: 97.0 per cent to 103.0 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: practically insoluble in water, very soluble in ethanol (96 per cent) and in methylene chloride.

IDENTIFICATION

A. Melting point (*2.2.14*): 34 °C to 38 °C.

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

TESTS

Appearance of solution. The solution is clear (*2.2.1*) and not more intensely coloured than reference solution Y_6 (*2.2.2, Method II*).

Dissolve 0.20 g in 10 ml of *methanol R*.

Specific optical rotation (*2.2.7*): + 35.0 to + 40.0 (dried substance).

Dissolve 0.200 g in *anhydrous ethanol R* and dilute to 20.0 ml with the same solvent.

Impurities A, B, C. Thin-layer chromatography (*2.2.27*).

Test solution. Dissolve 50 mg of the substance to be examined in *methylene chloride R* and dilute to 5.0 ml with the same solvent.

Reference solution (a). Dilute 1.0 ml of the test solution to 10.0 ml with *methylene chloride R*.

Reference solution (b). Dilute 1.0 ml of reference solution (a) to 10.0 ml with *methylene chloride R*.

Reference solution (c). Dilute 1.0 ml of reference solution (a) to 20.0 ml with *methylene chloride R*.

Reference solution (d). Dissolve 5 mg of *nandrolone decanoate for system suitability CRS* (containing impurities A, B, C) in 0.5 ml of *methylene chloride R*.

Plate: *TLC silica gel plate R*.

Mobile phase: *acetone R, heptane R* (30:70 *V/V*).

Application: 10 µl of the test solution and reference solutions (b), (c) and (d).

Development: over 2/3 of the plate.

Drying: in air.

Detection: treat with *alcoholic solution of sulphuric acid R* and heat at 130 °C until the spots appear. Examine in ultraviolet light at 366 nm.

Retardation factors: nandrolone decanoate = about 0.37; impurity A = about 0.45; impurity B = about 0.55; impurity C = about 0.58.

System suitability: reference solution (d):

– the chromatogram shows 4 clearly separated spots.

Limits:

– *impurity A*: any spot due to impurity A is not more intense than the principal spot in the chromatogram obtained with reference solution (b) (1.0 per cent);

– *impurities B, C*: any spot due to impurity B or C is not more intense than the principal spot in the chromatogram obtained with reference solution (c) (0.5 per cent).

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 25 mg of the substance to be examined in *methanol R* and dilute to 10.0 ml with the same solvent.

Reference solution (a). Dilute 1.0 ml of the test solution to 100.0 ml with *methanol R*. Dilute 1.0 ml of this solution to 10.0 ml with *methanol R*.