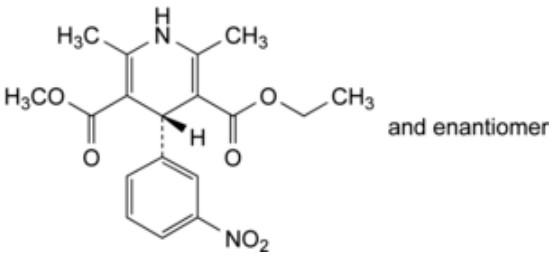
Edition: BP 2025 (Ph. Eur. 11.6 update)

Nitrendipine

General Notices

(Ph. Eur. monograph 1246)



and enantiomer

$C_{18}H_{20}N_2O_6$ 360.4 *39562-70-4*

Action and use

Calcium channel blocker.

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DEFINITION

Ethyl methyl (4*RS*)-2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate.

Content

98.5 per cent to 101.5 per cent (dried substance).

CHARACTERS

Appearance

Yellow, crystalline powder.

Solubility

Practically insoluble in water, freely soluble in ethyl acetate, sparingly soluble in anhydrous ethanol and in methanol.

It shows polymorphism (5.9).

Exposure to ultraviolet light leads to the formation of a nitrophenylpyridine derivative.

Prepare solutions immediately before use either protected from light or under long-wavelength light (> 420 nm).

IDENTIFICATION

Infrared absorption spectrophotometry (2.2.24).

Comparison nitrendipine CRS.

If the spectra obtained in the solid state show differences, record new spectra using 20 g/L solutions in methylene chloride R and a 0.2 mm cell.

TESTS

Related substances

Liquid chromatography (2.2.29).

Test solution Dissolve 20 mg of the substance to be examined in 2.5 mL of tetrahydrofuran R and dilute to 10.0 mL with the mobile phase.

Reference solution (a) Dilute 1.0 mL of the test solution to 100.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 10.0 mL with the mobile phase.

Reference solution (b) Dissolve 15.0 mg of nitrendipine impurity A CRS in 2.5 mL of tetrahydrofuran R and dilute to 10.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 20.0 mL with the mobile phase.

Reference solution (c) Dilute 0.5 mL of the test solution to 20.0 mL with the mobile phase.

Reference solution (d) Mix 1.0 mL of reference solution (b) and 1.0 mL of reference solution (c), then dilute to 25.0 mL with the mobile phase.

Reference solution (e) Dissolve 2 mg of nitrendipine for peak identification CRS (containing impurities B and C) in 0.5 mL of tetrahydrofuran R and dilute to 1.0 mL with the mobile phase.

Column:

— *size*: *l* = 0.125 m, Ø = 4 mm;

— *stationary phase*: irregular octadecylsilyl silica gel for chromatography R (5 µm);

— *temperature*: 40 °C.

Mobile phase acetonitrile R, tetrahydrofuran R, water R (14:22:64 *V/V/V*).

Flow rate 1 mL/min.

Detection Spectrophotometer at 235 nm.

Injection 10 µL of the test solution and reference solutions (a), (d) and (e).

Run time 5 times the retention time of nitrendipine.

Identification of impurities Use the chromatogram supplied with *nitrendipine for peak identification CRS* and the chromatogram obtained with reference solution (e) to identify the peaks due to impurities B and C; use the chromatogram obtained with reference solution (d) to identify the peak due to impurity A.

Relative retention With reference to nitrendipine (retention time = about 9 min): impurity B = about 0.7; impurity A = about 0.8; impurity C = about 1.4.

System suitability Reference solution (d):

— *resolution*: minimum 2.0 between the peaks due to impurity A and nitrendipine.

Limits:

— *impurities B, C*: for each impurity, not more than 4 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.4 per cent);

— *impurity A*: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (d) (0.15 per cent);

— *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.10 per cent);

— *total*: maximum 0.7 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).

Loss on drying (*2.2.32*)

Maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.160 g with gentle heating if necessary in a mixture of 25 mL of *2-methyl-2-propanol R* and 25 mL of *perchloric acid solution R*. Titrate with *0.1 M cerium sulfate*, using 0.1 mL of *ferroin R* as indicator. Titrate slowly towards the end of the titration. Carry out a blank titration.

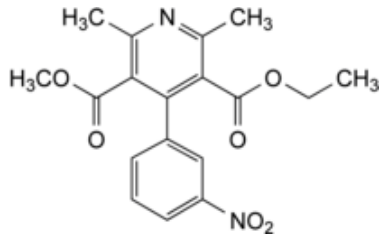
1 mL of *0.1 M cerium sulfate* is equivalent to 18.02 mg of $C_{18}H_{20}N_2O_6$.

STORAGE

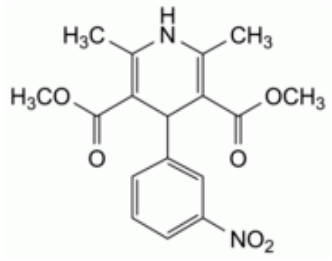
Protected from light.

IMPURITIES

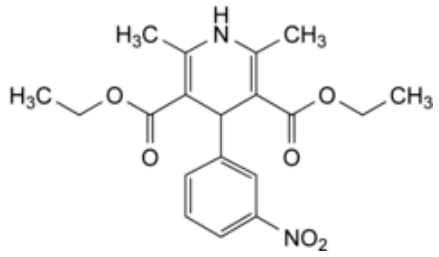
Specified impurities *A, B, C.*



A. ethyl methyl 2,6-dimethyl-4-(3-nitrophenyl)pyridine-3,5-dicarboxylate,



B. dimethyl 2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate,



C. diethyl 2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate.

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