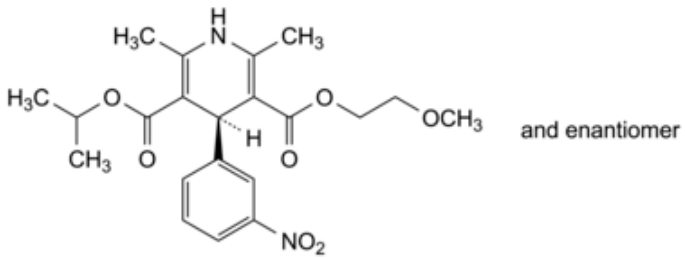
https://nhathuocngocanh.com/bp

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

Nimodipine

General Notices

(Ph. Eur. monograph 1245)



and enantiomer

$C_{21}H_{26}N_2O_7$ 418.4 *66085-59-4*

Action and use

Calcium channel blocker.

Preparations

Nimodipine Infusion

Nimodipine Tablets

Ph Eur

DEFINITION

2-Methoxyethyl 1-methylethyl (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

www.webofpharma.com

https://nhathuocngocanh.com/bp

Light yellow or yellow, crystalline powder.

Solubility

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

It shows polymorphism (*5.9*).

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

IDENTIFICATION

A. Optical rotation (see Tests).
B. Infrared absorption spectrophotometry (*2.2.24*).

Comparison *nimodipine 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

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

Solution S

Dissolve 1.0 g in *acetone R* and dilute to 20.0 mL with the same solvent.

Appearance of solution

Solution S is clear (*2.2.1*).

Optical rotation (*2.2.7*)

-0.10° to + 0.10°, determined on solution S.

Related substances

Liquid chromatography (*2.2.29*).

Test solution Dissolve 40 mg of the substance to be examined in 2.5 mL of *tetrahydrofuran R* and dilute to 25.0 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 4 mg of *nimodipine for peak identification CRS* (containing impurity C) in 0.25 mL of *tetrahydrofuran R* and dilute to 2.5 mL with the mobile phase.

Reference solution (c) Dilute 0.5 mL of the test solution to 25.0 mL with the mobile phase. Mix 0.5 mL of this solution with 0.5 mL of *nimodipine impurity A CRS* and dilute to 10.0 mL with the mobile phase.

Column:

www.webofpharma.com

https://nhathuocngocanh.com/bp

— *size*: *l* = 0.125 m, Ø = 4.6 mm;

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

— *temperature*: 40 °C.

Mobile phase *methanol R*, *tetrahydrofuran R*, *water R* (20:20:60 *V/V/V*).

Flow rate 2.0 mL/min.

Detection Spectrophotometer at 235 nm.

Injection 20 µL.

Run time 4.5 times the retention time of nimodipine.

Identification of impurities Use the chromatogram supplied with *nimodipine for peak identification CRS* and the chromatogram obtained with reference solution (b) to identify the peak due to impurity C; use the chromatogram obtained with reference solution (c) to identify the peak due to impurity A.

Relative retention With reference to nimodipine (retention time = about 7 min): impurity C = about 0.5; impurity A = about 0.9.

System suitability Reference solution (c):

— *peak-to-valley ratio*: minimum 4.0, 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 nimodipine.

Limits:

— *impurity C*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 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*: not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 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

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

Dissolve with gentle heating 0.180 g in a mixture of 25 mL of *2-methyl-2-propanol R* and 25 mL of *perchloric acid solution R*. Add 0.1 mL of *ferroin R*. Titrate with *0.1 M cerium sulfate*. Titrate slowly towards the end of the titration. Carry out a blank titration.

www.webofpharma.com

https://nhathuocngocanh.com/bp

1 mL of *0.1 M cerium sulfate* is equivalent to 20.92 mg of $C_{21}H_{26}N_2O_7$.

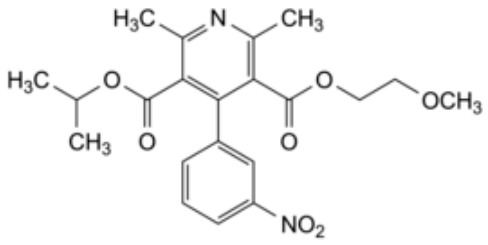
STORAGE

Protected from light.

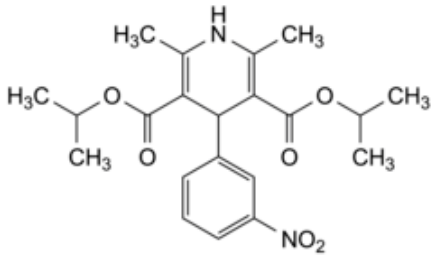
IMPURITIES

Specified impurities C.

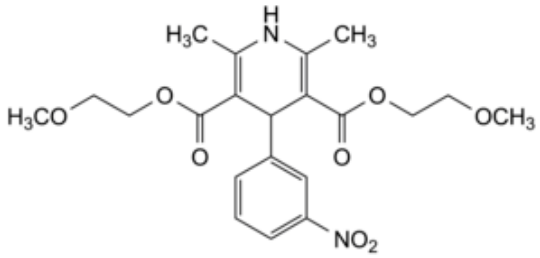
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical 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) A, B.



A. 2-methoxyethyl 1-methylethyl 2,6-dimethyl-4-(3-nitrophenyl)pyridine-3,5-dicarboxylate,



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



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

www.webofpharma.com