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

Nifedipine Oral Suspension

General Notices

NOTE: This monograph has been developed to cover unlicensed formulations.

Action and use

Calcium channel blocker.

DEFINITION

Nifedipine Oral Suspension is a suspension of Nifedipine in a suitable vehicle.

The oral suspension complies with the requirements stated under Oral Liquids and with the following requirements. Where appropriate, the oral suspension also complies with the requirements stated under Unlicensed Medicines.

Content of nifedipine, $C_{17}H_{18}N_2O_6$

90.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) Shake a quantity of the oral suspension containing 1 mg of Nifedipine with sufficient of a solution containing equal volumes of *dichloromethane* and *methanol* to produce 5 mL.
(2) 0.02% w/v of *nifedipine BPCRS* in equal volumes of *dichloromethane* and *methanol*.
(3) Equal volumes of solutions (1) and (2).

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel F_{254}* (Merck silica gel 60 F_{254} plates are suitable).
(b) Use the mobile phase as described below.
(c) Apply 20 µL of each solution.
(d) Develop the plate to 15 cm in an unsaturated tank.
(e) After removal of the plate, allow it to dry in air and examine under *ultraviolet light (254 nm* and *366 nm*).

MOBILE PHASE

4 volumes of *ethyl acetate* and 6 volumes of *cyclohexane*.

SYSTEM SUITABILITY

The test is not valid unless the principal spot in the chromatogram obtained with solution (3) appears as a single compact spot.

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) is similar in position and size to that in the chromatogram obtained with solution (2).

B. In the Assay, the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the principal peak in the chromatogram obtained with solution (2).

TESTS

Dissolution

Complies with the requirements stated under Unlicensed Medicines, Oral Suspensions. Use a volume of the oral suspension containing one dose.

Impurities A and B

Carry out the method for *liquid chromatography,* Appendix III D, using the following solutions.

(1) Disperse a quantity of the oral suspension containing 5 mg of Nifedipine in 10 mL of *methanol*, shake for 15 minutes, add sufficient *methanol* to produce 20 mL and filter through a 0.45-µm nylon filter.
(2) 0.000125% w/v of *dimethyl 2,6-dimethyl-4-(2-nitrophenyl)pyridine-3,5-dicarboxylate BPCRS* (impurity A) in the mobile phase.
(3) 0.000125% w/v of *dimethyl 2,6-dimethyl-4-(2-nitrosophenyl)pyridine-3,5-dicarboxylate BPCRS* (impurity B) in the mobile phase.
(4) Dilute 1 volume of solution (1) to 100 volumes with the mobile phase; mix 1 volume of the resulting solution with 1 volume of solution (2) and 1 volume of solution (3).

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (LiChrospher RP is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 235 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

9 volumes of *acetonitrile*, 36 volumes of *methanol* and 55 volumes of *water*.

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to nifedipine (retention time, about 27.3 minutes) are: impurity A, about 0.63; impurity B, about 0.79.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4):

the *resolution* between the peaks due to impurity A and impurity B is at least 1.5;

the *resolution* between the peaks due to impurity B and nifedipine is at least 1.5;

if there is a peak with a relative retention of about 0.74 with reference to nifedipine (propyl parahydroxybenzoate), the *peak-to-valley ratio* is at least 5.0, where *Hp* is the height above the baseline of the peak due to impurity B and *Hv* is the height above the baseline of the lowest point of the curve separating this peak from the peak due to propyl parahydroxybenzoate.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to dimethyl 2,6-dimethyl-4-(2-nitrophenyl)pyridine-3,5-dicarboxylate (impurity A) is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

the area of any peak corresponding to dimethyl 2,6-dimethyl-4-(2-nitrosophenyl)pyridine-3,5-dicarboxylate (impurity B) is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (0.5%).

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Disperse a weighed quantity of the oral suspension containing 1 mg of Nifedipine in 9 mL of a mixture containing 1 volume of *acetonitrile* and 4 volumes of *methanol* and shake for 15 minutes. Add sufficient water to produce 20 mL, shake for a further 15 minutes and filter through a 0.45-µm nylon filter.

(2) Dissolve 25 mg of *nifedipine BPCRS* in a mixture containing 4.5 mL of *acetonitrile* and 18 mL of *methanol*. Add sufficient *water* to produce 50 mL and dilute 1 volume to 10 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Impurities A and B may be used.

DETERMINATION OF CONTENT

Determine the *weight per mL* of the oral suspension, Appendix V G, and calculate the content of $C_{17}H_{18}N_2O_6$, weight in volume, using the declared content of $C_{17}H_{18}N_2O_6$ in *nifedipine BPCRS*.

STORAGE

Nifedipine Oral Suspension should be protected from light.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities A and B listed under Nifedipine.