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Nifedipine Prolonged-release Capsules

General Notices

Prolonged-release Nifedipine Capsules

Details for the public consultation of this monograph are as follows:

EAG/Panel/Working Party	Medicinal Chemicals 1
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Deadline for Comment	31st December 2024
Target Publication Date (subject to change)	BP 2026
Notes	**Revised monograph** If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required. **Related substances** Limits revised. Named impurities - additional information added for clarity.

Nifedipine Prolonged-release Capsules from different manufacturers, whilst complying with the requirements of the monograph, are not interchangeable unless otherwise justified and authorised.

Action and use

Calcium channel blocker.

DEFINITION

Nifedipine Prolonged-release Capsules contain Nifedipine. They are formulated so that the medicament is released over a period of several hours.

PRODUCTION

A suitable dissolution test is carried out to demonstrate the appropriate release of Nifedipine. The dissolution profile reflects the *in vivo* performance which in turn is compatible with the dosage schedule recommended by the manufacturer.

The capsules comply with the requirements stated under Capsules and with the following requirements.

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

95.0 to 105.0% of the stated amount.

Carry out all the following procedures in the dark or under long-wavelength light (greater than 420 nm). Prepare solutions immediately before use and protect them from light.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) Shake a quantity of the contents of the capsules containing 20 mg of Nifedipine with 100 mL of a solution containing equal volumes of *dichloromethane* and *methanol* and filter through a Whatman GF/C filter.
(2) 0.02% w/v of *nifedipine BPCRS* in equal volumes of *dichloromethane* and *methanol*.
(3) Equal volumes of solution (1) and solution (2).

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel* GF_{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, dry in air and examine under *ultraviolet light (254 nm)*.

MOBILE PHASE

40 volumes of *ethyl acetate* and 60 volumes of *cyclohexane*.

SYSTEM SUITABILITY

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

CONFIRMATION

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

B. In the Assay, the chromatogram obtained with solution (1) shows a peak with the same retention time as the principal peak in the chromatogram obtained with solution (2).

TESTS

Related substances

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

(1) Shake a quantity of the powdered content of the capsules containing 50 mg of Nifedipine in 15 mL of *methanol*, dilute to 25 mL with *methanol* and filter. Dilute 1 volume of the resulting solution with 1 volume of the mobile phase.
(2) Dilute 1 volume of solution (1) to 100 volumes with the mobile phase and further dilute 1 volume of the resulting solution to 5 volumes with the mobile phase.

(3) 0.0005% w/v of *dimethyl-2,6-dimethyl-4-(2-nitrophenyl)pyridine-3,5-dicarboxylate BPCRS* (nifedipine impurity A) in the mobile phase.
(4) 0.0005% w/v of *dimethyl-2,6-dimethyl-4-(2-nitrosophenyl)pyridine-3,5-dicarboxylate BPCRS* (nifedipine impurity B) in the mobile phase.
(5) Dilute 1 volume of solution (1) to 100 volumes with the mobile phase and further dilute 1 volume of the resulting solution with 1 volume of solution (3) and 1 volume of solution (4).
(6) Dilute 1 volume of solution (2) to 2 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Lichrosorb RP18 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*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (5):

the *resolution factor* between the peaks due to dimethyl-2,6-dimethyl-4-(2-nitrophenyl)pyridine-3,5-dicarboxylate (nifedipine impurity A) and dimethyl-2,6-dimethyl-4-(2-nitrosophenyl)pyridine-3,5-dicarboxylate (nifedipine impurity B) is at least 1.5;

the *resolution factor* between the peaks due to dimethyl-2,6-dimethyl-4-(2-nitrosophenyl)pyridine-3,5-dicarboxylate (nifedipine impurity B) and nifedipine is at least 1.5.

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 (nifedipine impurity A)* is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (0.5%);

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

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of the areas of any *secondary peaks* is not greater than 10 times the area of the principal peak in the chromatogram obtained with solution (2) (2.0%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (6) (0.1%).

ASSAY

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

(1) To a quantity of the powdered mixed contents of 20 capsules containing 50 mg of Nifedipine, add 15 mL of *methanol*, dilute to 50 mL with *methanol* and filter. Dilute 1 volume of the resulting solution to 5 volumes with the mobile phase.
(2) 0.02% w/v *nifedipine BPCRS* in the mobile phase.
(3) 0.0003% w/v of *nifedipine BPCRS*, 0.0002% w/v of *dimethyl-2,6-dimethyl-4-(2-nitrophenyl)pyridine-3,5-dicarboxylate BPCRS* (nifedipine impurity A) and 0.0002% w/v of *dimethyl-2,6-dimethyl-4-(2-nitrosophenyl)pyridine-3,5-dicarboxylate BPCRS* (nifedipine impurity B) in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless in solution (3):

the *resolution factor* between the peaks due to dimethyl-2,6-dimethyl-4-(2-nitrophenyl)pyridine-3,5-dicarboxylate (nifedipine impurity A) and dimethyl-2,6-dimethyl-4-(2-nitrosophenyl)pyridine-3,5-dicarboxylate (nifedipine impurity B)is at least 1.5;

the *resolution factor* between the peaks due to dimethyl-2,6-dimethyl-4-(2-nitrosophenyl)pyridine-3,5-dicarboxylate (nifedipine impurity B) and nifedipine is at least 1.5.

DETERMINATION OF CONTENT

Calculate the content of $C_{17}H_{18}N_2O_6$ in the capsules using the declared content of $C_{17}H_{18}N_2O_6$ in *nifedipine BPCRS*.

IMPURITIES

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