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

Nimodipine Infusion

General Notices

Nimodipine Intravenous Infusion

Action and use

Calcium channel blocker.

DEFINITION

Nimodipine Infusion is a sterile solution containing Nimodipine in a suitable aqueous alcoholic solvent. It is supplied as a ready-to-use solution.

The infusion complies with the requirements stated under Parenteral Preparations and with the following requirements.

Content of nimodipine, $C_{21}H_{26}N_2O_7$

95.0 to 105.0% of the stated amount.

Carry out the following procedures protected from light or under long-wavelength light (greater than 420 nm). Prepare the 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) Extract a volume of the infusion containing 4 mg of Nimodipine with 4 mL of *dichloromethane* and use the dichloromethane layer.
(2) 0.1% w/v solution of *nimodipine BPCRS* in *dichloromethane*.
(3) A mixture of equal volumes of solution (1) and solution (2).

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel F_{254}* (Merck HPTLC silica gel 60 F_{254} plates are suitable).
(b) Use the mobile phase as described below.
(c) Apply 10 µL of each solution as bands.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, allow it to dry in air and examine under *ultraviolet light (254 nm)*. Spray the plate with a freshly prepared 0.1% w/v solution of *2,6-dichloroquinonechlorimide* in *ethanol* and heat at 110° for about 3 minutes.

MOBILE PHASE

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

CONFIRMATION

The bands due to nimodipine are brownish-green to bluish-green.

The principal band in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

The principal band in the chromatogram obtained with solution (3) appears as a single compact band.

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

TESTS

Acidity or alkalinity

pH, 6.0 to 7.5, Appendix V L.

Bacterial endotoxins

The endotoxin limit concentration is 5.0 IU per mL, Appendix XIV C.

Related substances

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

(1) Dilute a volume of the infusion, if necessary, with *absolute ethanol*, to contain 0.02% w/v of Nimodipine.
(2) Dilute 1 volume of solution (1) to 100 volumes with the mobile phase and dilute 2 volumes of this solution to 10 volumes with the mobile phase.
(3) 0.0001% w/v of *nimodipine impurity A BPCRS* in *absolute ethanol*.
(4) 0.0001% w/v each of *nimodipine BPCRS* and *nimodipine impurity A BPCRS* in *absolute ethanol*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (12.5 cm × 4.0 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Lichrospher RP-18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use a column temperature of 30°.
(e) Use a detection wavelength of 235 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

12 volumes of *acetonitrile*, 24 volumes of *tetrahydrofuran* and 64 volumes of *water*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution factor* between the peaks due to nimodipine and nimodipine impurity A is at least 1.5 and the *symmetry factor* of the peak due to nimodipine is not more than 2.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to nimodipine 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 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* other than any peak corresponding to impurity A is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%).

Disregard any peak with an area less than 0.25 times the area of the principal peak in the chromatogram obtained with solution (2) (0.05%).

ASSAY

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

(1) Dilute a volume of the infusion, if necessary, with *absolute ethanol*, to produce a solution containing 0.02% w/v of Nimodipine.
(2) 0.02% w/v of *nimodipine BPCRS* in *absolute ethanol*.
(3) 0.0001% w/v each of *nimodipine BPCRS* and *nimodipine impurity A BPCRS* in *absolute ethanol*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution factor* between the two principal peaks is at least 1.3 and the *symmetry factor* of the peak due to nimodipine is not more than 2.0.

DETERMINATION OF CONTENT

Calculate the content of $C_{21}H_{26}N_2O_7$ in the infusion using the declared content of $C_{21}H_{26}N_2O_7$ in *nimodipine BPCRS*.

STORAGE

Nimodipine Infusion should be protected from light. It should not be allowed to come into contact with polyvinyl chloride (PVC).

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Nimodipine.