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Felodipine Prolonged-release Tablets

General Notices

Prolonged-release Felodipine Tablets

Felodipine Prolonged-release Tablets 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

Felodipine Prolonged-release Tablets contain Felodipine. 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 Felodipine. The dissolution profile reflects the *in vivo* performance which in turn is compatible with the dosage schedule recommended by the manufacturer.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of felodipine, $C_{18}H_{19}Cl_2NO_4$

92.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Extract a quantity of the powdered tablets containing 15 mg of Felodipine with 100 mL of *ethanol (96%)*, filter, and dilute 5 mL of the filtrate to 50 mL with *ethanol (96%)*. The *light absorption*, Appendix II B, in the range 250 to 450 nm exhibits a maximum at 362 nm.
B. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) Shake a quantity of the powdered tablets containing 10 mg of Felodipine with 10 mL of *methanol* and filter through a 0.45-µm filter.
(2) 0.1% w/v of *felodipine BPCRS* in *methanol*.
(3) 0.1% w/v each of *felodipine BPCRS* and *nifedipine BPCRS* in *methanol*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating substance *silica gel F_{254}*.
(b) Use the mobile phase described below.
(c) Apply 10 µL of each solution.
(d) Develop to 15 cm.
(e) Dry the plate 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) shows two clearly separated spots of different colours.

CONFIRMATION

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

C. In the Assay, the chromatogram obtained with solution (1) shows a principal 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.

Prepare a mixture of 0.08% w/v of *orthophosphoric acid R* and 0.8% w/v of *sodium dihydrogen orthophosphate* (solvent A).

(1) Mix with the aid of ultrasound a quantity of the powdered tablets containing 10 mg of Felodipine with 10 mL of *methanol* and 20 mL of *acetonitrile* for 5 minutes, add 15 mL of solvent A and continue to disperse with the aid of ultrasound for a further 30 minutes. Cool, dilute to 50 mL with solvent A and filter through a 0.45-µm PTFE filter.
(2) Dilute 1 volume of solution (1) to 100 volumes with the mobile phase.
(3) Dilute 1 volume of solution (2) to 10 volumes with the mobile phase.
(4) 0.006% w/v of *felodipine impurity standard BPCRS* in mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 3.9 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Waters Nova-Pak is suitable).
(b) Use isocratic elution using the mobile phase described below.
(c) Use a flow rate of 1.0 mL per minute.
(d) Use ambient column temperature.
(e) Use a detection wavelength of 254 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

20 volumes of *methanol*, 40 volumes of *acetonitrile* and 40 volumes of solvent A.

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to felodipine (retention time about 7 minutes) are: impurity B, about 0.7; impurity A, about 0.9; impurity C, about 1.4.

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 felodipine is at least than 2.5.

LIMITS

Identify any peaks corresponding to impurities A, B and C in the chromatogram obtained with solution (1), using the chromatogram obtained with solution (4), and multiply the area of the peak due to impurity A by a correction factor of 2.3.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to Impurity A is not greater than four times the area of the principal peak in the chromatogram obtained with solution (2) (4.0%);

the sum of the areas of the peaks corresponding to impurity B and impurity C is not greater than the area of the principal peak in the chromatogram obtained with solution (2);

the area of any other *secondary peak* is not greater than twice the area of the principal peak in the chromatogram obtained with solution (3) (0.2%);

the sum of the areas of any other *secondary peaks* is not greater than 0.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%).

ASSAY

Prepare a mixture of 0.08% w/v of *orthophosphoric acid R* and 0.8% w/v of *sodium dihydrogen orthophosphate* (solvent A).

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Mix with the aid of ultrasound a quantity of the powdered tablets containing 10 mg of Felodipine with 10 mL of methanol and 20 mL of *acetonitrile* for 5 minutes, add 15 mL of solvent A and mix with the aid of ultrasound for a further 30 minutes. Cool, add sufficient solvent A to produce 50 mL and filter through a 0.45-µm PTFE filter. Dilute 1 volume of the resulting solution to 10 volumes with the mobile phase.
(2) 0.002% w/v of *felodipine BPCRS* in mobile phase.
(3) 0.006% w/v of *felodipine impurity standard BPCRS* in mobile phase.

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* between the peaks due to impurity A and felodipine is at least 2.5.

DETERMINATION OF CONTENT

Calculate the content of $C_{18}H_{19}Cl_2NO_4$ in the tablets using the declared content of $C_{18}H_{19}Cl_2NO_4$ in *felodipine BPCRS*.

IMPURITIES

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