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

Diclofenac Diethylamine Gel

General Notices

Action and use

Cyclo-oxygenase inhibitor; analgesic; anti-inflammatory.

DEFINITION

Diclofenac Diethylamine Gel contains Diclofenac Diethylamine in a suitable basis.

The gel complies with the requirements stated under Topical Semi-solid Preparations and with the following requirements.

Content of diclofenac diethylamine, $C_{18}H_{22}Cl_2N_2O_2$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.

(1) To a quantity of the gel containing 50 mg of Diclofenac Diethylamine, add 12.5 mL of *methanol* and mix with the aid of ultrasound for 10 minutes. Dilute to 25 mL with *methanol*, filter (a 0.45-µm PVDF is suitable) and use the filtrate.
(2) 0.2% w/v of *diclofenac diethylamine BPCRS* in *methanol*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating high performance silica gel (Merck silica gel 60 HPTLC plates are suitable).
(b) Use the mobile phase as described below.
(c) Apply 20 µL of each solution.
(d) Develop the plate to 8 cm.
(e) After removal of the plate, dry at 105° for 30 minutes. Spray with *ninhydrin solution* and heat at 105° for 45 minutes.

MOBILE PHASE

1 volume of *hydrochloric acid*, 1 volume of *water*, 6 volumes of *glacial acetic acid* and 11 volumes of *ethyl acetate*.

CONFIRMATION

The two principal spots in the chromatogram obtained with solution (1) correspond in position and colour to those 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 gel containing 50 mg of Diclofenac Diethylamine with 50 mL of *acetone* for 10 minutes, filter and evaporate the filtrate to dryness under reduced pressure. Dissolve the residue in 10 mL of a mixture of 40 volumes of *water* and 60 volumes of *methanol*, dilute 1 volume of this solution to 5 volumes with the mobile phase and filter through a glass fibre filter (Whatman GF/C is suitable).
(2) Dilute 1 volume of solution (1) to 100 volumes with the mobile phase.
(3) 0.1% w/v of *diclofenac for system suitability EPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (YMC-Pack Pro C18 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 254 nm.
(f) Inject 20 µL of each solution.
(g) For solution (1) allow the chromatography to proceed for 1.6 times the retention time of diclofenac.

MOBILE PHASE

34 volumes of a mixture of equal volumes of a 0.1% w/v solution of *orthophosphoric acid* and a 0.16% w/v solution of *sodium dihydrogen orthophosphate*, previously adjusted to pH 2.5 with *orthophosphoric acid*, and 66 volumes of *methanol*.

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to diclofenac (retention time about 25 minutes) are: impurity A, about 0.4 and impurity F, about 0.8.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity F and diclofenac is at least 4.0.

LIMITS

Identify any peaks due to impurities A and F in the chromatogram obtained with solution (1) using the chromatogram obtained with solution (3). Multiply the area of any peak corresponding to impurity A by a correction factor of 0.7 and any peak corresponding to impurity F by a correction factor of 0.3.

In the chromatogram obtained with solution (1):

the area of any *secondary peak* is not greater than half the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

the sum of the areas of any *secondary peaks* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1%).

Disregard any peak with an area less than 0.05 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) Shake a quantity of the gel containing 50 mg of Diclofenac Diethylamine with 50 mL of *acetone* for 10 minutes, filter and evaporate the filtrate to dryness under reduced pressure. Dissolve the residue in 100 mL of a mixture of 40 volumes of *water* and 60 volumes of *methanol*, dilute 1 volume of this solution to 10 volumes with the mobile phase and filter through a glass fibre filter (Whatman GF/C is suitable).
(2) 0.05% w/v of *diclofenac sodium BPCRS* in *methanol*. Dilute 1 volume of the resulting solution to 10 volumes using the mobile phase.
(3) 0.1% w/v of *diclofenac sodium BPCRS* and 0.1% w/v of *diclofenac impurity A BPCRS* in *methanol*. Dilute 1 volume of the resulting solution to 10 volumes using the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped octylsilyl silica gel for chromatography* (5 µm) (end-capped Zorbax C8 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 254 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

20 volumes of a mixture of equal volumes of a 0.1% w/v solution of *orthophosphoric acid* and a 0.16% w/v solution of *sodium dihydrogen orthophosphate*, adjusted to pH 2.5, and 80 volumes of *methanol*.

When the chromatograms are recorded under the prescribed conditions, the retention times are about 5 minutes for diclofenac and about 4 minutes for impurity A.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to diclofenac and impurity A is at least 2.0.

DETERMINATION OF CONTENT

Calculate the content of $C_{18}H_{22}Cl_2N_2O_2$ in the gel using the declared content of $C_{14}H_{10}Cl_2NNaO_2$ in *diclofenac sodium BPCRS*. Each mg of $C_{14}H_{10}Cl_2NNaO_2$ is equivalent to 1.1609 mg of $C_{18}H_{22}Cl_2N_2O_2$.