Diclofenac Gel

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

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Notes	Revised monograph If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required. **Definition; Content** Revised to include both salt forms: diclofenac diethylamine and diclofenac sodium. **Related Substances** Correction factors for impurities A and F added. Column, mobile phase and system suitability updated.

Diclofenac Gel prepared from Diclofenac Diethylamine is not necessarily interchangeable with Diclofenac Gel prepared from Diclofenac Sodium.

Action and use

Cyclo-oxygenase inhibitor; analgesic; anti-inflammatory.

DEFINITION

Diclofenac Gel contains Diclofenac Diethylamine or Diclofenac Sodium in a suitable basis.

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

Content of diclofenac, $C_{14}H_{11}Cl_2N_2O_2$

95.0 to 105.0% of the stated amount of diclofenac.

IDENTIFICATION

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

(1) Add to a quantity of the gel containing the equivalent of 25 mg of diclofenac 12.5 mL of *methanol* and mix with the aid of ultrasound for 10 minutes. Dilute to 25 mL with *methanol*. Filter and use the filtrate.(0.45µm PVDF is suitable)

(2) 0.1% w/v of *diclofenac diethylamine BPCRS* in *methanol*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *octadecasilyl silica gel for HPTLC* (Merck silica gel 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 110° 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 the equivalent of 50 mg of diclofenac 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* (containing impurities A and F) 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 1.5 times the retention time of diclofenac.

MOBILE PHASE

34 volumes of a mixture of equal volumes of a 0.05% w/v solution of *orthophosphoric acid* and a 0.08% 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 corresponding to diclofenac impurity F and diclofenac is at least 4.0.

LIMITS

Identify the peaks due to impurity A using the chromatogram obtained with solution (3) and multiply the area of the peak by a correction factor of 0.7. Identify the peak due to impurity F using the relative retention time and multiply the area of the peak 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 the equivalent of 50 mg of diclofenac 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 diclofenac impurity A.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution factor* between the peaks corresponding to diclofenac and diclofenac 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 $C_{18}H_{22}Cl_2N_2O_2$.

IMPURITIES

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