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

Diclofenac Prolonged-release Capsules

General Notices

Prolonged-release Diclofenac Capsules

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

DEFINITION

Diclofenac Prolonged-release Capsules contain Diclofenac Sodium. 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 Diclofenac Sodium. 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 diclofenac sodium, $C_{14}H_{10}Cl_2NNaO_2$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Add 0.5 mL of *glacial acetic acid* and 15 mL of *methanol* to a quantity of the powdered capsule contents containing 0.15 g of Diclofenac Sodium and mix with the aid of ultrasound for 40 minutes. Shake gently for 1 minute, filter and collect the filtrate in 15 mL of *water*. Filter the precipitate (Whatman GF/C is suitable) under reduced pressure, wash with four 5-mL quantities of *water* and dry at 105° for 2 to 3 hours. The *infrared absorption spectrum* of the dried precipitate, Appendix II A, is concordant with the *reference spectrum* of diclofenac *(RS 096)*.

TESTS

Related substances

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

To 30 volumes of *acetonitrile for chromatography* add 70 volumes of *water* (solvent A).

(1) Add 30 mL of solvent A to a quantity of the powdered contents of the capsules containing 0.1 g of Diclofenac Sodium and mix with the aid of ultrasound for 10 minutes with occasional shaking. Cool, add sufficient solvent A to produce 50 mL and filter (Whatman GF/C is suitable).
(2) Dilute 1 volume of solution (1) to 100 volumes with solvent A and dilute 1 volume of this solution to 5 volumes with solvent A.
(3) 0.0005% w/v of *diclofenac sodium BPCRS* and 0.0005% w/v of *diclofenac impurity A BPCRS* in solvent A.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4 mm) packed with *base-deactivated, end-capped octylsilyl silica gel for chromatography* (5 µm) (Lichrospher RP Select B or equivalent 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 ambient column temperature.
(e) Use a detection wavelength of 230 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

A mixture of 5 volumes of *tetrahydrofuran*, 30 volumes of *acetonitrile* and 65 volumes of 0.05M *ammonium dihydrogen orthophosphate*, previously adjusted to pH 5.0 using 18M *ammonia*.

When the chromatograms are recorded under the prescribed conditions, the retention times are about 18 minutes for diclofenac and about 26 minutes for diclofenac impurity A. Continue the chromatography for 5 times the retention time of diclofenac.

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 4.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of any *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 all the *secondary peaks* 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

Dissolve 6.8 g of *potassium dihydrogen orthophosphate* in 1000 mL of *water* and adjust the pH to 6.8 with 1M *sodium hydroxide* (solution A). To a quantity of the mixed contents of 20 capsules containing 100 mg of Diclofenac Sodium add 10 mL of *ethanol (96%)* and mix with the aid of ultrasound for 20 minutes or until completely dispersed. Add 150 mL of solution A and mix with the aid of ultrasound for a further 20 minutes or until completely dispersed. Cool to room temperature, dilute to 250 mL with solution A and shake thoroughly. Filter the resulting solution and dilute 5 mL to 100 mL with solution A. Prepare a reference standard in the following manner. Dissolve 50 mg of *diclofenac sodium BPCRS* in 10 mL of *ethanol (96%)* with the aid of ultrasound for 5 minutes. Add 150 mL of solution A and mix with the aid of ultrasound for a further 5 minutes. Cool to room temperature, dilute to 250 mL with solution A and shake thoroughly. Dilute 5 mL of the resulting solution to 50 mL with solution A. Measure the *absorbance*, Appendix II B, of the solutions at 275 nm using in the reference cell a 0.4% v/v solution of *ethanol (96%)* in solution A.

Calculate the content of $C_{14}H_{10}Cl_2NNaO_2$ in the capsules using the *absorbances* at the maximum at 275 nm and the declared content of $C_{14}H_{10}Cl_2NNaO_2$ in *diclofenac sodium BPCRS*.

STORAGE

Diclofenac Prolonged-release Capsules should be protected from moisture.

IMPURITIES

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