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

Diclofenac Prolonged-release Tablets

General Notices

Prolonged-release Diclofenac Tablets

Diclofenac 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

Cyclo-oxygenase inhibitor; analgesic; anti-inflammatory.

DEFINITION

Diclofenac Prolonged-release Tablets 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 tablets comply with the requirements stated under Tablets 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

Remove the coating from 10 tablets and powder the cores. To a quantity of the powdered tablet cores containing 0.15 g of Diclofenac Sodium, add 0.5 mL of *glacial acetic acid* and 15 mL of *methanol* and mix with the aid of ultrasound. Shake gently for 1 minute, filter and collect the filtrate in 15 mL of *water*. Filter the precipitate under reduced pressure (Whatman GF/C filter paper is suitable), 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.

(1) Shake a quantity of the powdered tablets containing 50 mg of Diclofenac Sodium with 70 mL of the mobile phase for 30 minutes, add sufficient of the mobile phase to produce 100 mL, mix, centrifuge an aliquot and filter the supernatant liquid through a 0.45-µm filter.

(2) Dilute 1 volume of solution (1) to 100 volumes with the mobile phase and dilute 1 volume of this solution to 5 volumes with the mobile phase.
(3) 0.0005% w/v of *diclofenac sodium BPCRS* and 0.0005% w/v of *diclofenac impurity A BPCRS* 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) 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 0.1% w/v solution of *orthophosphoric acid* and a 0.16% w/v solution of *sodium dihydrogen orthophosphate*, adjusted to pH 2.5, and 66 volumes of *methanol*.

When the chromatograms are recorded under the prescribed conditions, the relative retention times 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 factor* between the peaks corresponding to diclofenac and diclofenac impurity A is at least 6.5.

LIMITS

Identify the peak 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 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

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

(1) To a quantity of the powdered tablets containing 0.5 g of Diclofenac Sodium add 800 mL of *methanol* and mix with the aid of ultrasound. Dilute the resulting solution with the mobile phase to produce a solution containing 0.005% w/v of Diclofenac Sodium.
(2) 0.005% w/v of *diclofenac sodium BPCRS* in the mobile phase.
(3) 0.0005% w/v of *diclofenac sodium BPCRS* and 0.0005% w/v of *diclofenac impurity A BPCRS* in 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) (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 *phosphoric 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* between the peaks corresponding to diclofenac and diclofenac impurity A is at least 2.0.

DETERMINATION OF CONTENT

Calculate the content of $C_{14}H_{10}Cl_2NNaO_2$ in the tablets using the declared content of $C_{14}H_{10}Cl_2NNaO_2$ in *diclofenac sodium BPCRS*.

STORAGE

Diclofenac Prolonged-release Tablets should be protected from moisture.

IMPURITIES

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