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Diclofenac Gastro-resistant Tablets

General Notices

Diclofenac Tablets

Gastro-resistant Diclofenac Tablets

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. **Identification B** new test added. **Dissolution** new test added. **Related substances** quantitative limits introduced & limits revised **Assay** amendments made.

Action and use

Cyclo-oxygenase inhibitor; analgesic; anti-inflammatory.

DEFINITION

Diclofenac Gastro-resistant Tablets contain Diclofenac Sodium. They are covered with a gastro-resistant coating or prepared from granules or particles covered with a gastro-resistant coating.

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

A. Remove the coating from 10 tablets and powder the cores. Add 0.5 mL of *glacial acetic acid* and 15 mL of *methanol* to a quantity of the powdered tablet cores containing 0.15 g of Diclofenac Sodium 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 (a 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)*.
B. Yields the reactions characteristic of *sodium salts*, Appendix VI.

TESTS

Dissolution

Carry out the *dissolution test for tablets and capsules*, Appendix XII B1.

First stage

(a) Use Apparatus 2, rotating the basket at 50 revolutions per minute.
(b) Use 900 mL of 0.1M *hydrochloric acid*, at a temperature of 37°, as the medium.

PROCEDURE

Solution A 1 volumes of 5M *sodium hydroxide* and 45 volumes of 0.1M *hydrochloric acid*.

(1) After 2 hours, transfer the tablets to individual vessels for the Final stage test. Add 20 mL of 5M *sodium hydroxide* to the remaining medium in each vessel, mix and withdraw a sample of the medium and filter. Measure the *absorbance* of the filtrate, Appendix II B, diluted with solution A , if necessary, at 276 nm using solution A in the reference cell.
(2) Measure the *absorbance* of a 0.00136% w/v solution of *diclofenac sodium BPCRS* in solution A using solution A in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of diclofenac sodium, $C_{14}H_{14}O_3$, in the medium using the declared content of $C_{14}H_{10}Cl_2NNaO_2$ in *diclofenac sodium BPCRS*.

LIMITS

The amount of diclofenac sodium released is not more than 10% of the stated amount.

Final stage

Buffer pH 6.8 1 volume of 7.6% w/v of anhydrous trisodium orthophosphate and 3 volumes of 0.1M *hydrochloric acid*, adjust the pH to 6.8, if necessary, with 2M *hydrochloric acid* or 2M *sodium hydroxide*.

(a) Use Apparatus 2, rotating the basket at 50 revolutions per minute.
(b) Use 900 mL of buffer pH 6.8, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 45 minutes, withdraw a sample of the medium and filter. Measure the *absorbance* of the filtrate, Appendix II B, diluted with the dissolution medium, if necessary, to produce a solution expected to contain 0.00204% w/v of Diclofenac Sodium, at 276 nm using the dissolution medium in the reference cell.
(2) Measure the *absorbance* of a 0.00204% w/v solution of *diclofenac sodium BPCRS* in the dissolution medium.

DETERMINATION OF CONTENT

Calculate the total content of diclofenac sodium, $C_{14}H_{14}O_3$, in the final stage medium using the declared content of $C_{14}H_{10}Cl_2NNaO_2$ in *diclofenac sodium BPCRS*.

LIMITS

The amount of diclofenac sodium released is not less than 75% (Q) of the stated amount.

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, 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) Dissolve the contents of a vial of *diclofenac for system suitability EPCRS* in 1 mL of 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 1.6 times the retention time of diclofenac.

MOBILE PHASE

34 volumes of a solution containing 0.05% w/v of *orthophosphoric acid* and 0.08% w/v of *sodium dihydrogen orthophosphate*, previously adjusted to pH 2.5 with *orthophosphoric acid*, and 66 volumes

of *methanol*.

SYSTEM SUITABILITY

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

CALCULATION OF IMPURITIES

For each impurity, use the concentration of diclofenac sodium in solution (2).

For the reporting threshold, use the concentration of diclofenac sodium in solution (2).

For peak identification, use solution (3).

Diclofenac retention time: about 25 minutes.

Relative retention: impurity A, about 0.4; impurity F, about 0.8.

Correction factors: impurity A, multiply by 0.7; impurity F, multiply by 0.3.

LIMITS

— unspecified impurities: for each impurity, not more than 0.2%;

— total unspecified impurities: not more than 0.5%;

— reporting threshold: 0.1%.

ASSAY

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

(1) Shake 10 tablets with 700 mL of *methanol (50%)* for 30 minutes with the aid of ultrasound, add sufficient mobile phase to produce 1000 mL, centrifuge an aliquot and filter the supernatant liquid through a 0.45-µm filter. Dilute the filtrate 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.

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 solution containing 0.05% w/v of *orthophosphoric acid* and 0.08% w/v of *sodium dihydrogen orthophosphate*, previously adjusted to pH 2.5 with *orthophosphoric acid*, and 80 volumes of *methanol*.

When the chromatograms are recorded under the prescribed conditions, the retention time of diclofenac is about 5 minutes.

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*.

Supporting information for Assay

Geometric scaling of column dimensions and chromatographic parameters to the validated Assay method conditions have been explored in order to reduce the solvent needed and the environmental impact. The "More resources" tab, available in the BP online monograph, provides additional information on the investigations carried out. Visit https://www.pharmacopoeia.com/guidance/environmentalhub for more information.

STORAGE

Diclofenac Gastro-resistant Tablets should be protected from moisture.

IMPURITIES

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