Ciprofibrate Tablets

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

EAG/Panel/Working Party	Medicinal Chemicals 2
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Notes	New monograph If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required.

Action and use

Fibrate; lipid-regulating drug.

DEFINITION

Ciprofibrate Tablets contain Ciprofibrate.

The tablets complies with the requirements stated under Tablets and with the following requirements.

Content of ciprofibrate, $C_{13}H_{14}Cl_2O_3$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

In the Assay, record the UV spectrum of the principal peak in the chromatograms obtained with solutions (1) and (2) with a diode array detector in the range of 210 to 400 nm.

The UV spectrum of the principal peak in the chromatogram obtained with solution (1) is concordant with that of the peak in the chromatogram obtained with solution (2);

the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the peak in the chromatogram obtained with solution (2).

TESTS

Dissolution

Comply with the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 50 revolutions per minute.

(b) Use 900 mL of 0.05M *sodium dihydrogen orthophosphate dihydrate*, adjusted to pH 7.0 with 5M *sodium hydroxide*, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 45 minutes withdraw a sample of the medium and measure the *absorbance* of the filtered sample, suitably diluted with the dissolution medium, to produce a solution containing 0.0011% w/v of Ciprofibrate, at the maximum at 236 nm, Appendix II B, using dissolution medium in the reference cell.

(2) Measure the *absorbance* of a 0.0011% w/v solution of *ciprofibrate BPCRS* in the dissolution medium using dissolution medium in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of ciprofibrate, $C_{13}H_{14}Cl_2O_3$, in the medium from the absorbances obtained and using the declared content of $C_{13}H_{14}Cl_2O_3$ in *ciprofibrate BPCRS*.

LIMITS

The amount of ciprofibrate 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 prepared in the mobile phase.

(1) Mix with the aid of ultrasound a quantity of powdered tablets containing 0.2 g of Ciprofibrate with 50 mL of the mobile phase. Dilute to produce 100 mL and filter (Whatman No. 1 paper is suitable).

(2) Dilute 1 volume of solution (1) to 100 volumes. Further dilute 1 volume to 5 volumes.

(3) 0.25% w/v of *ciprofibrate for system suitability EPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Spherisorb ODS2 is suitable).

(b) Use isocratic elution and the mobile phase described below.

(c) Use a flow rate of 2 mL per minute.

(d) Use a column temperature of 35°.

(e) Use a detection wavelength of 230 nm.

(f) Inject 20 µL of each solution.

(g) Allow the chromatography to proceed for 6 times the retention time of ciprofibrate.

MOBILE PHASE

50 volumes of *acetonitrile* and 50 volumes of 0.1% w/v of *orthophosphoric acid*.

SYSTEM SUITABILITY

For system suitability, use solution (3):

the *resolution* between the peaks due to impurity A and impurity B is at least 1.5.

CALCULATION OF IMPURITIES

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

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

For peak identification, use solution (3).

Ciprofibrate retention time: about 5 minutes.

Relative retention: impurity A, about 0.6; impurity B, about 0.7; impurity D, about 3.0; impurity E, about 4.5.

Correction factors: impurity A, multiply by 1.3.

LIMITS

— impurity E: not more than 0.80%;

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

— total impurities: not more than 1.0%;

— reporting threshold: 0.1%.

ASSAY

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

(1) Mix with the aid of ultrasound a quantity of the powdered tablets containing 0.2 g of Ciprofibrate with 100 mL of *acetonitrile*. Allow to cool and add sufficient *acetonitrile* to produce 200 mL. Filter (Whatman No. 1 paper is suitable) and dilute 1 volumes of the filtrate to 20 volumes with the mobile phase.

(2) 0.1% w/v of *ciprofibrate BPCRS* in *acetonitrile*. Dilute 1 volume to 20 volumes with the mobile phase to produce a solution containing 0.005% w/v of *ciprofibrate BPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (1), the number of *theoretical plates* is not less than 2,200.

DETERMINATION OF CONTENT

Calculate the content of ciprofibrate, $C_{13}H_{14}Cl_2O_3$, in the tablets from the chromatograms obtained and using the declared content of $C_{13}H_{14}Cl_2O_3$ in *ciprofibrate BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities A, B, D and E listed under Ciprofibrate.