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

Bezafibrate Tablets

General Notices

Action and use

Fibrate; lipid-regulating drug.

DEFINITION

Bezafibrate Tablets contain Bezafibrate.

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

Content of bezafibrate, $C_{19}H_{20}ClNO_4$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of the powdered tablets containing 0.2 g of Bezafibrate with two 10-mL quantities of *acetone* for 10 minutes, combine and filter the extracts (a Whatman GF/C is suitable) and evaporate the filtrate to dryness. The infrared absorption spectrum of the residue, Appendix II A, is concordant with the reference spectrum of bezafibrate *(RS 419)*.

TESTS

Dissolution

Comply with the requirements for Monographs of the British Pharmacopoeia in 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 as the medium, at a temperature of 37°, 900 mL of a pH 6.5 buffer solution prepared by dissolving 0.608 g of *sodium hydroxide* and 6.805 g of *potassium dihydrogen orthophosphate* in sufficient *water* to produce 1000 mL and adjusting the pH to 6.5 ± 0.05 using *sodium hydroxide solution* or *orthophosphoric acid*.

PROCEDURE

(1) After 45 minutes withdraw a 10 mL sample of the medium, filter and dilute 1 volume of the filtrate to 20 volumes with the dissolution medium and measure the *absorbance* at the maximum at 229 nm, Appendix II B, using dissolution medium in the reference cell.
(2) Measure the *absorbance* of a 0.0011% w/v solution of *bezafibrate BPCRS* in the dissolution medium using dissolution medium in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of bezafibrate, $C_{19}H_{20}ClNO_4$, in the medium from the absorbances obtained and using the declared content of $C_{19}H_{20}ClNO_4$ in *bezafibrate BPCRS*.

Related substances

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 100 mg of Bezafibrate with 15 mL of *methanol* for 2 minutes, shake for a further 10 minutes, cool, add sufficient of the mobile phase to produce 100 mL, mix and filter, discarding the first 20 mL of filtrate.
(2) Dilute 1 volume of solution (1) to 200 volumes with the mobile phase.
(3) Dilute 1 volume of solution (2) to 10 volumes with the mobile phase.
(4) Dissolve sufficient quantities of *bezafibrate BPCRS* and c*hlorobenzoyltyramine BPCRS* in the minimum quantity of *methanol* and dilute with mobile phase to produce a solution containing 0.0002% w/v of *bezafibrate BPCRS* and 0.0002% w/v of *chlorobenzoyltyramine BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 3.9 mm) packed with *octadecylsilyl silica gel for chromatography* (4 µm) (Novapak 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 239 nm.
(f) Inject 20 µL of each solution.
(g) The retention time of bezafibrate is about 5 minutes. Allow the chromatography to proceed for four times the retention time of the principal peak.

MOBILE PHASE

3.9 volumes of 40% w/v of *tetrabutylammonium hydroxide*, 400 volumes of *acetonitrile* and 600 volumes of *water* and adjusting the final pH to 4.0 with 10% v/v *orthophosphoric acid*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution factor* between the peaks due to bezafibrate and chlorobenzoyltyramine is at least 7.0. If necessary, adjust the content of tetrabutylammonium hydroxide to obtain the required resolution.

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) (0.5%);

the total area of any such peaks is not greater than 1.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.75%).

Disregard any peak with an area less than that of the principal peak in the chromatogram obtained with solution (4) (0.05%).

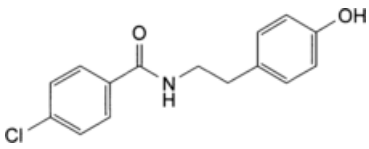
ASSAY

Weigh and powder 20 tablets. For solution (1) mix with the aid of ultrasound a quantity of the powdered tablets containing 100 mg of Bezafibrate with 70 mL of *methanol* for 2 minutes, shake for a further 10 minutes, cool, add sufficient *methanol* to produce 100 mL, mix and filter discarding the first 20 mL of filtrate; dilute 1 volume of the filtrate to 100 volumes with *methanol*. Solution (2) contains 0.001% w/v of *bezafibrate BPCRS* in *methanol*.

Measure the *absorbance* at the maximum at 229 nm, Appendix II B. Calculate the content of $C_{19}H_{20}ClNO_4$ in the tablets from the absorbances obtained and from the declared content of $C_{19}H_{20}ClNO_4$ in *bezafibrate BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include,



4-chloro-*N*-[2-(4-hydroxyphenyl)ethyl]benzamide (chlorobenzoyltyramine).