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Bezafibrate Prolonged-release Tablets

General Notices

Prolonged-release Bezafibrate Tablets

Bezafibrate 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

Fibrate; lipid-regulating drug.

DEFINITION

Bezafibrate Prolonged-release Tablets contain Bezafibrate. 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 bezafibrate. 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 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, filter the combined extracts (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

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 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) Dissolve sufficient quantities of *bezafibrate BPCRS* and *chlorobenzoyltyramine 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*.

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(4) Dilute 1 volume of solution (2) to 10 volumes with the mobile phase.

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 ambient column temperature.
(e) Use a detection wavelength of 230 nm.
(f) Inject 20 µL of each solution.

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

A mixture of 3.9 volumes of a 40% w/v solution of *tetrabutylammonium hydroxide*, 400 volumes of *acetonitrile* and 600 volumes of *water*, 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 (3), 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) (0.01%).

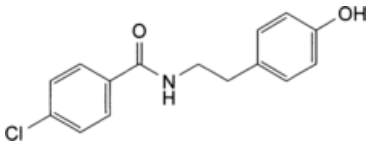
ASSAY

Weigh and powder 20 tablets. For solution (1) mix with the aid of ultrasound a quantity of the powdered tablets containing 0.1 g 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 to 100 volumes with *methanol*. Solution (2) is a 0.001% w/v solution of *bezafibrate BPCRS* in *methanol*.

Measure the *absorbance* of the resulting solutions at the maximum at about 230 nm, Appendix II B. Calculate the content of $C_{19}H_{20}ClNO_4$ 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).

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