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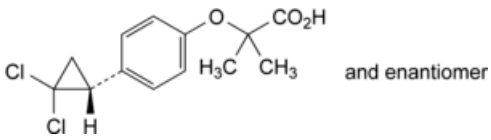
Edition: BP 2025 (Ph. Eur. 11.6 update)

Ciprofibrate

General Notices

(Ph. Eur. monograph 2013)



and enantiomer

$C_{13}H_{14}Cl_2O_3$ 289.2 *52214-84-3*

Action and use

Fibrate; lipid-regulating drug.

Preparation

Ciprofibrate Tablets

Ph Eur

DEFINITION

2-[4-[(1*RS*)-2,2-Dichlorocyclopropyl]phenoxy]-2-methylpropanoic acid.

Content

99.0 per cent to 101.0 per cent (anhydrous substance).

CHARACTERS

Appearance

White or slightly yellow, crystalline powder.

Solubility

Practically insoluble in water, freely soluble in anhydrous ethanol, soluble in toluene.

mp

About 115 °C.

IDENTIFICATION

Infrared absorption spectrophotometry (2.2.24).

Comparison ciprofibrate CRS.

TESTS

Appearance of solution

The solution is clear (2.2.1) and not more intensely coloured than reference solution BY_4 (2.2.2, Method II).

Dissolve 1.0 g in anhydrous ethanol R and dilute to 10.0 mL with the same solvent.

Related substances

Liquid chromatography (2.2.29).

Solvent mixture acetonitrile R, water R (50:50 *V/V*).

Test solution Dissolve 0.125 g of the substance to be examined in the solvent mixture and dilute to 50.0 mL with the solvent mixture.

Reference solution (a) Dilute 1.0 mL of the test solution to 100.0 mL with the solvent mixture. Dilute 1.0 mL of this solution to 10.0 mL with the solvent mixture.

Reference solution (b) Dissolve the contents of a vial of ciprofibrate for system suitability B CRS (containing impurities A, C and E) in 2 mL of the solvent mixture.

Column:

— *size*: *l* = 0.15 m, Ø = 4.6 mm;

— *stationary phase*: end-capped octylsilyl silica gel for chromatography R (5 µm).

Mobile phase:

— *mobile phase A*: 1.36 g/L solution of potassium dihydrogen phosphate R adjusted to pH 2.2 with phosphoric acid R;

— *mobile phase B*: acetonitrile for chromatography R;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 30	75 → 30	25 → 70
30 - 40	30	70

Flow rate 1.5 mL/min.

Detection Spectrophotometer at 230 nm.

Injection 10 µL.

Identification of impurities Use the chromatogram supplied with ciprofibrate for system suitability B CRS and the chromatogram obtained with reference solution (b) to identify the peaks due to impurities A, C and E.

Relative retention With reference to ciprofibrate (retention time = about 19 min): impurity A = about 0.7; impurity C = about 0.95; impurity E = about 1.5.

System suitability Reference solution (b):

— *resolution*: minimum 3.0 between the peaks due to impurity C and ciprofibrate.

Calculation of percentage contents:

— *correction factor*: multiply the peak area of impurity A by 2.3;

— for each impurity, use the concentration of ciprofibrate in reference solution (a).

Limits:

— *impurity E*: maximum 0.5 per cent;

— *impurity A*: maximum 0.10 per cent;

— *unspecified impurities*: for each impurity, maximum 0.10 per cent;

— *total*: maximum 0.7 per cent;

— *reporting threshold*: 0.05 per cent.

Chlorides (*2.4.4*)

Maximum 350 ppm.

To 0.190 g add 20 mL of *water R* and sonicate for 8 min. Filter. 15 mL of the filtrate complies with the test.

Water (*2.5.12*)

Maximum 0.5 per cent, determined on 1.000 g.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.250 g in a mixture of 20 mL of *water R* and 40 mL of *anhydrous ethanol R*. Titrate with *0.1 M sodium hydroxide*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M sodium hydroxide* is equivalent to 28.92 mg of $C_{13}H_{14}Cl_2O_3$.

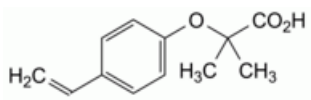
STORAGE

In an airtight container, protected from light.

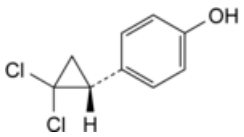
IMPURITIES

Specified impurities *A, E*.

Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical use (2034). It is therefore not necessary to identify these impurities for demonstration of compliance. See also 5.10. Control of impurities in substances for pharmaceutical use) *B, C, D*.

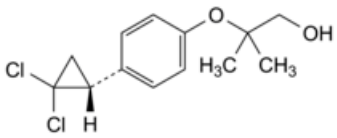


A. 2-[4-(ethenyl)phenoxy]-2-methylpropanoic acid,



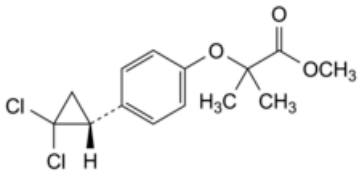
and enantiomer

B. 4-[(1*RS*)-2,2-dichlorocyclopropyl]phenol,



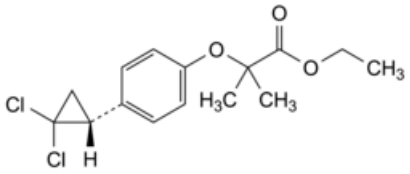
and enantiomer

C. 2-[4-[(1*RS*)-2,2-dichlorocyclopropyl]phenoxy]-2-methylpropan-1-ol,



and enantiomer

D. methyl 2-[4-[(1*RS*)-2,2-dichlorocyclopropyl]phenoxy]-2-methylpropanoate,



and enantiomer

E. ethyl 2-[4-[(1*RS*)-2,2-dichlorocyclopropyl]phenoxy]-2-methylpropanoate.

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