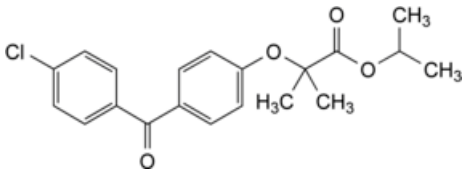
Edition: BP 2025 (Ph. Eur. 11.6 update)

Fenofibrate

General Notices

(Ph. Eur. monograph 1322)



$C_{20}H_{21}ClO_4$ 360.8 *49562-28-9*

Action and use

Fibrate; lipid-regulating drug.

Preparations

Fenofibrate Capsules

Fenofibrate Tablets

Ph Eur

DEFINITION

1-Methylethyl 2-[4-(4-chlorobenzoyl)phenoxy]-2-methylpropanoate.

Content

98.0 per cent to 102.0 per cent (dried substance).

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Practically insoluble in water, very soluble in methylene chloride, slightly soluble in ethanol (96 per cent).

IDENTIFICATION

A. Melting point (2.2.14): 79 °C to 82 °C.
B. Infrared absorption spectrophotometry (2.2.24).

Comparison *fenofibrate CRS*.

TESTS

Solution S

To 5.0 g, add 25 mL of *distilled water R* and heat at 50 °C for 10 min. Cool and dilute to 50.0 mL with *distilled water R*. Filter. Use the filtrate as solution S.

Appearance of solution

The solution is clear (2.2.1) and not more intensely coloured than reference solution BY_6 (2.2.2, *Method II*).

Dissolve 0.50 g in *acetone R* and dilute to 10.0 mL with the same solvent.

Acidity

Dissolve 1.0 g in 50 mL of *ethanol (96 per cent) R* previously neutralised using 0.2 mL of *phenolphthalein solution R1*. Not more than 0.2 mL of *0.1 M sodium hydroxide* is required to change the colour of the indicator to pink.

Related substances

Liquid chromatography (2.2.29).

Test solution Dissolve 0.100 g of the substance to be examined in the mobile phase and dilute to 100.0 mL with the mobile phase.

Reference solution (a) Dissolve 25.0 mg of *fenofibrate CRS* in the mobile phase and dilute to 25.0 mL with the mobile phase.

Reference solution (b) Dissolve 5.0 mg of *fenofibrate CRS*, 5.0 mg of *fenofibrate impurity A CRS*, 5.0 mg of *fenofibrate impurity B CRS* and 10.0 mg of *fenofibrate impurity G CRS* in the mobile phase and dilute to 100.0 mL with the mobile phase. Dilute 1.0 mL of the solution to 50.0 mL with the mobile phase.

Column:

— *size*: *l* = 0.25 m, Ø = 4.0 mm;

— *stationary phase*: *octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase Mix 30 volumes of *water R* acidified to pH 2.5 with *phosphoric acid R* and 70 volumes of *acetonitrile R*.

Flow rate 1 mL/min.

Detection Spectrophotometer at 286 nm.

Injection 20 µL of the test solution and reference solution (b).

Run time Twice the retention time of fenofibrate.

Identification of impurities Use the chromatogram obtained with reference solution (b) to identify the peaks due to impurities A, B and G.

Relative retention With reference to fenofibrate (retention time = about 10 min): impurity A = about 0.34; impurity B = about 0.36; impurity G = about 1.35.

System suitability Reference solution (b):

— *resolution*: minimum 1.5 between the peaks due to impurities A and B.

Limits:

— *impurities A, B*: for each impurity, not more than 1.5 times the area of the corresponding peak in the chromatogram obtained with reference solution (b) (0.15 per cent);

— *impurity G*: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (b) (0.2 per cent);

— *unspecified impurities*: for each impurity, not more than the area of the peak due to fenofibrate in the chromatogram obtained with reference solution (b) (0.10 per cent);

— *total*: not more than 5 times the area of the peak due to fenofibrate in the chromatogram obtained with reference solution (b) (0.5 per cent);

— *disregard limit*: 0.5 times the area of the peak due to fenofibrate in the chromatogram obtained with reference solution (b) (0.05 per cent).

Halides expressed as chlorides (*2.4.4*)

Maximum 100 ppm.

To 5 mL of solution S add 10 mL of *distilled water R*.

Sulfates (*2.4.13*)

Maximum 100 ppm, determined on solution S.

Loss on drying (*2.2.32*)

Maximum 0.5 per cent, determined on 1.000 g by drying *in vacuo* at 60 °C.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Liquid chromatography (*2.2.29*) as described in the test for related substances with the following modifications.

Injection 5 µL of the test solution and reference solution (a).

System suitability Reference solution (a):

— *repeatability*: maximum relative standard deviation of 1.0 per cent determined on 6 injections.

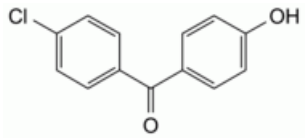
STORAGE

Protected from light.

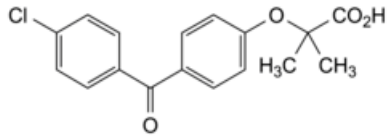
IMPURITIES

Specified impurities *A, B, G.*

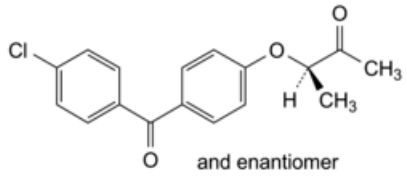
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical 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) *C, D, E, F.*



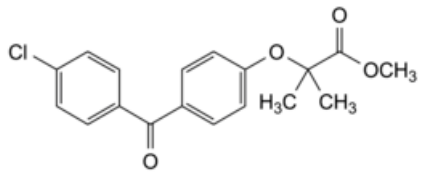
A. (4-chlorophenyl)(4-hydroxyphenyl)methanone,



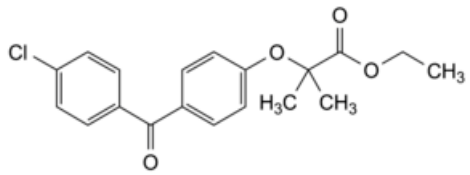
B. 2-[4-(4-chlorobenzoyl)phenoxy]-2-methylpropanoic acid (fenofibric acid),



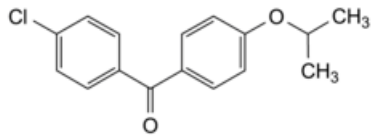
C. (3*RS*)-3-[4-(4-chlorobenzoyl)phenoxy]butan-2-one,



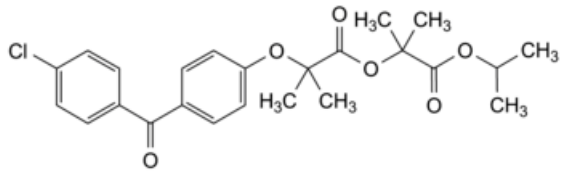
D. methyl 2-[4-(4-chlorobenzoyl)phenoxy]-2-methylpropanoate,



E. ethyl 2-[4-(4-chlorobenzoyl)phenoxy]-2-methylpropanoate,



F. (4-chlorophenyl)[4-(1-methylethoxy)phenyl]methanone,



G. 1-methylethyl 2-[[2-[4-(4-chlorobenzoyl)phenoxy]-2-methylpropanoyl]oxy]-2-methylpropanoate.

Ph Eur