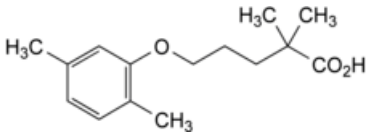
Edition: BP 2025 (Ph. Eur. 11.6 update)

Gemfibrozil

General Notices

(Ph. Eur. monograph 1694)



$C_{15}H_{22}O_3$ 250.3 *25812-30-0*

Action and use

Fibrate; lipid-regulating drug.

Preparations

Gemfibrozil Capsules

Gemfibrozil Tablets

Ph Eur

DEFINITION

5-(2,5-Dimethylphenoxy)-2,2-dimethylpentanoic acid.

Content

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

CHARACTERS

Appearance

White or almost white, waxy, crystalline powder.

Solubility

Practically insoluble in water, very soluble in methylene chloride, freely soluble in anhydrous ethanol and in methanol.

IDENTIFICATION

A. Melting point (2.2.14): 58 °C to 61 °C.
B. Infrared absorption spectrophotometry (2.2.24).

Comparison gemfibrozil CRS.

TESTS

Related substances

Liquid chromatography (2.2.29).

Test solution Dissolve 40.0 mg of the substance to be examined in mobile phase A and dilute to 10.0 mL with mobile phase A.

Reference solution (a) Dissolve the contents of a vial of gemfibrozil for system suitability CRS (containing impurities C, D and E) in 2.0 mL of acetonitrile R.

Reference solution (b) Dilute 1.0 mL of the test solution to 100.0 mL with mobile phase A. Dilute 1.0 mL of this solution to 10.0 mL with mobile phase A.

Reference solution (c) Dissolve 5 mg of 2,5-dimethylphenol R (impurity A) in mobile phase A and dilute to 10.0 mL with mobile phase A.

Column:

— *size*: *l* = 0.25 m, Ø = 4.0 mm;

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

Mobile phase:

— *mobile phase A*: dissolve 0.49 g of potassium acetate R in 400 mL of water for chromatography R, adjust to pH 4.0 with phosphoric acid R and add 600 mL of acetonitrile R;

— *mobile phase B*: acetonitrile R;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 5	100	0
5 - 20	100 → 0	0 → 100
20 - 25	0	100

Flow rate 1.5 mL/min.

Detection Spectrophotometer at 276 nm.

Injection 20 µL.

Identification of impurities Use the chromatogram supplied with gemfibrozil for system suitability CRS and the chromatogram obtained with reference solution (a) to identify the peaks due to impurities C, D and E; use the chromatogram obtained with reference solution (c) to identify the peak due to impurity A.

Relative retention With reference to gemfibrozil (retention time = about 7 min): impurity A = about 0.4; impurity C = about 1.3; impurity D = about 1.5; impurity E = about 1.7; impurity I = about 2.0; impurity H = about 2.9.

System suitability Reference solution (a):

— resolution: minimum 6.0 between the peaks due to gemfibrozil and impurity C, and minimum 2.0 between the peaks due to impurities D and E.

Limits:

— *correction factors*: for the calculation of content multiply the peak areas of the following impurities by the corresponding correction factor: impurity A = 0.5; impurity D = 1.8; impurity E = 0.2; impurity H = 0.6;

— *impurities E, I*: for each impurity, not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent);

— *impurities A, D, H*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent);

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

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

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

Water (*2.5.12*)

Maximum 0.25 per cent, determined on 2.000 g.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 2.0 g. Allow to stand for 1 h after the first moistening before heating.

ASSAY

Dissolve 0.200 g in 40 mL of *methanol R*. Add 10 mL of *water R* and 1 mL of *0.1 M hydrochloric acid*. Carry out a potentiometric titration (*2.2.20*) using *0.1 M sodium hydroxide*. Read the volume added between the 2 points of inflexion.

1 mL of *0.1 M sodium hydroxide* is equivalent to 25.03 mg of $C_{15}H_{22}O_3$.

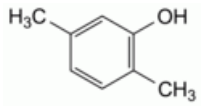
STORAGE

Protected from light.

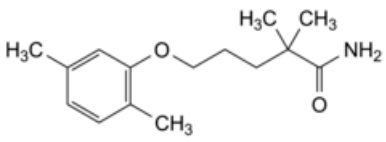
IMPURITIES

Specified impurities *A, D, E, H, I.*

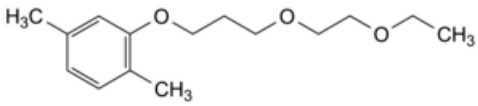
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical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



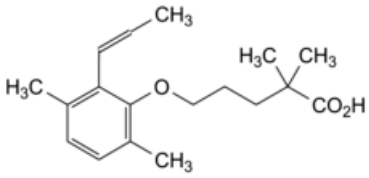
A. 2,5-dimethylphenol (*p*-xylenol),



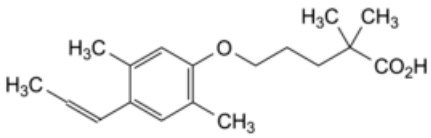
B. 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanamide,



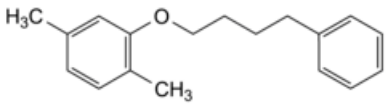
C. 2-[3-(2-ethoxyethoxy)propoxy]-1,4-dimethylbenzene,



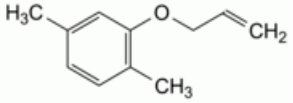
D. 5-[3,6-dimethyl-2-(prop-1-en-1-yl)phenoxy]-2,2-dimethylpentanoic acid,



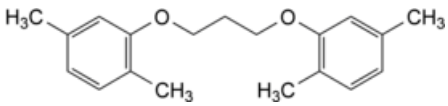
E. 5-[2,5-dimethyl-4-(prop-1-en-1-yl)phenoxy]-2,2-dimethylpentanoic acid,



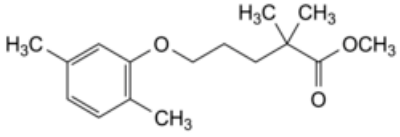
F. 1,4-dimethyl-2-(4-phenylbutoxy)benzene,



G. 1,4-dimethyl-2-(prop-2-en-1-yloxy)benzene,



H. 1,1′-[propane-1,3-diylbis(oxy)]bis(2,5-dimethylbenzene),



I. methyl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate.

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