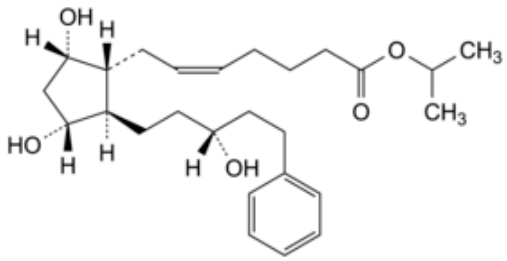
Edition: BP 2025 (Ph. Eur. 11.6 update)

Latanoprost

General Notices

(Ph. Eur. monograph 2230)



$C_{26}H_{40}O_5$ 432.6 *130209-82-4*

Action and use

Prostaglandin analogue; treatment of intraocular pressure

Ph Eur

DEFINITION

Propan-2-yl (5*Z*)-7-[(1*R*,2*R*,3*R*,5*S*)-3,5-dihydroxy-2-[(3*R*)-3-hydroxy-5-phenylpentyl]cyclopentyl]hept-5-enoate.

Content

94.0 per cent to 102.0 per cent (anhydrous substance).

CHARACTERS

Appearance

Clear, colourless or yellow, viscous, oily liquid.

Solubility

Practically insoluble in water, very soluble in acetonitrile, freely soluble in anhydrous ethanol.

IDENTIFICATION

A. Infrared absorption spectrophotometry (*2.2.24*).

Comparison *Ph. Eur. reference spectrum of latanoprost*.

B. Specific optical rotation (see Tests).

TESTS

Specific optical rotation (*2.2.7*)

+ 32.0 to + 37.0 (anhydrous substance).

Dissolve 0.100 g in *acetonitrile R* and dilute to 10.0 mL with the same solvent.

Related substances

Liquid chromatography (*2.2.29*). *Carry out the test protected from light.*

Test solution Dissolve 20.0 mg of the substance to be examined in 2 mL of *anhydrous ethanol R* and dilute to 10.0 mL with *heptane R*.

Reference solution (a) Dissolve the contents of a vial of *latanoprost for system suitability CRS* (containing impurities E and F) in 200 µL of *anhydrous ethanol R* then add 800 µL of *heptane R*.

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

Reference solution (c) Dissolve 20.0 mg of *latanoprost CRS* in 2 mL of *anhydrous ethanol R* and dilute to 10.0 mL with *heptane R*.

Column:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

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

— *temperature*: 30 °C.

Mobile phase *anhydrous ethanol R*, *heptane R* (6:94 *V/V*).

Flow rate 1.3 mL/min.

Detection Spectrophotometer at 210 nm.

Injection 10 µL of the test solution and reference solutions (a) and (b).

Run time Twice the retention time of latanoprost.

Identification of impurities Use the chromatogram supplied with *latanoprost for system suitability CRS* and the chromatogram obtained with reference solution (a) to identify the peaks due to impurities E and F.

Relative retention With reference to latanoprost (retention time = about 16 min): impurity E = about 0.9; impurity F = about 1.1.

System suitability Reference solution (a):

— *resolution*: minimum 2.0 between the peaks due to latanoprost and impurity F.

Calculation of percentage contents:

— for each impurity, use the concentration of latanoprost in reference solution (b).

Limits:

— *impurity F*: maximum 3.5 per cent;

— *impurity E*: maximum 0.4 per cent;

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

— *sum of impurities other than F*: maximum 1.0 per cent;

— *reporting threshold*: 0.05 per cent.

Impurity H

Liquid chromatography (2.2.29).

Solvent mixture acetonitrile R, water R (30:70 *V/V*).

Test solution Dissolve 25.0 mg of the substance to be examined in the solvent mixture and dilute to 25.0 mL with the solvent mixture.

Reference solution (a) Dissolve the contents of a vial of latanoprost impurity H CRS in 1.0 mL of the solvent mixture.

Reference solution (b) To 50 µL of the test solution add 450 µL of reference solution (a).

Column:

— *size*: *l* = 0.15 m, Ø = 4 mm;

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

— *temperature*: 60 °C.

Mobile phase:

— *mobile phase A*: phosphoric acid R, acetonitrile R1, water for chromatography R (0.1:30:70 *V/V/V*);

— *mobile phase B*: phosphoric acid R, water for chromatography R, acetonitrile R1 (0.1:20:80 *V/V/V*);

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 9	100	0
9 - 10	100 → 0	0 → 100
10 - 15	0	100

Flow rate 1.0 mL/min.

Detection Spectrophotometer at 200 nm.

Injection 50 µL.

Identification of impurities Use the chromatogram obtained with reference solution (a) to identify the peak due to impurity H.

Relative retention With reference to latanoprost (retention time = about 12 min): impurity H = about 0.7.

System suitability Reference solution (b):

— *resolution*: minimum 5.0 between the peaks due to impurity H and latanoprost.

Calculation of percentage content:

— use the concentration of impurity H in reference solution (a).

Limit:

— *impurity H*: maximum 0.15 per cent.

Water (*2.5.32*)

Maximum 0.50 per cent, determined on 0.100 g.

ASSAY

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

Injection Test solution and reference solution (c).

Calculate the percentage content of $C_{26}H_{40}O_5$ taking into account the assigned content of *latanoprost CRS*.

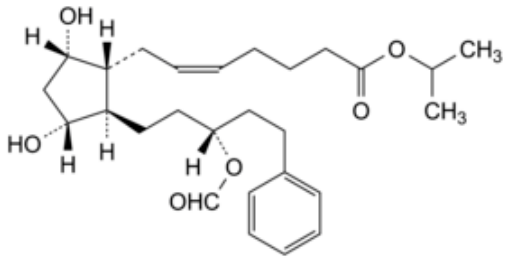
STORAGE

At a temperature of 2 °C to 8 °C.

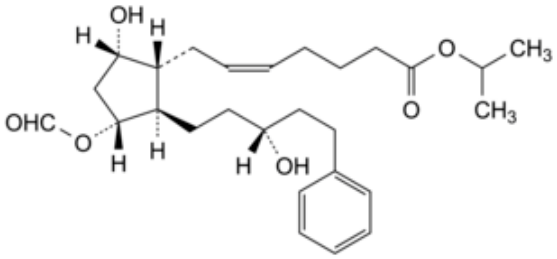
IMPURITIES

Specified impurities *E, F, H.*

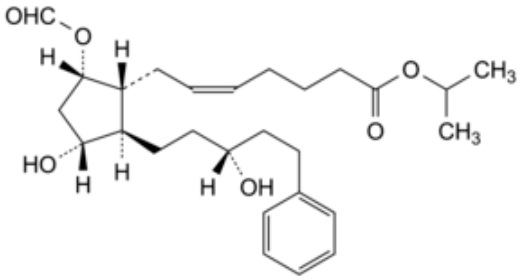
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical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



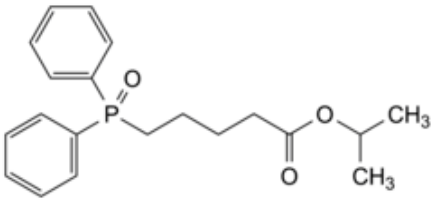
A. propan-2-yl (5*Z*)-7-[(1*R*,2*R*,3*R*,5*S*)-2-[(3*R*)-3-(formyloxy)-5-phenylpentyl]-3,5-dihydroxycyclopentyl]hept-5-enoate,



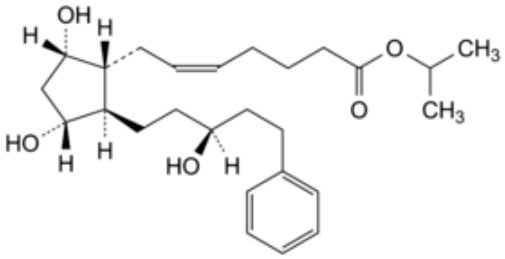
B. propan-2-yl (5*Z*)-7-[(1*R*,2*R*,3*R*,5*S*)-3-(formyloxy)-5-hydroxy-2-[(3*R*)-3-hydroxy-5-phenylpentyl]cyclopentyl]hept-5-enoate,



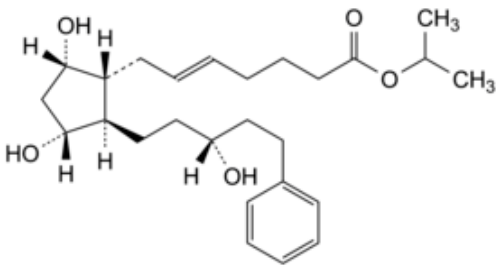
C. propan-2-yl (5*Z*)-7-[(1*R*,2*R*,3*R*,5*S*)-5-(formyloxy)-3-hydroxy-2-[(3*R*)-3-hydroxy-5-phenylpentyl]cyclopentyl]hept-5-enoate,



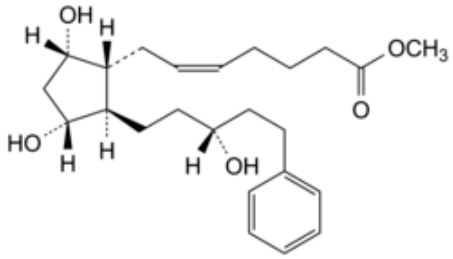
D. propan-2-yl 5-(diphenylphosphoryl)pentanoate,



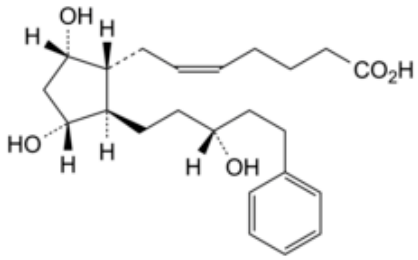
E. propan-2-yl (5*Z*)-7-[(1*R*,2*R*,3*R*,5*S*)-3,5-dihydroxy-2-[(3*S*)-3-hydroxy-5-phenylpentyl]cyclopentyl]hept-5-enoate,



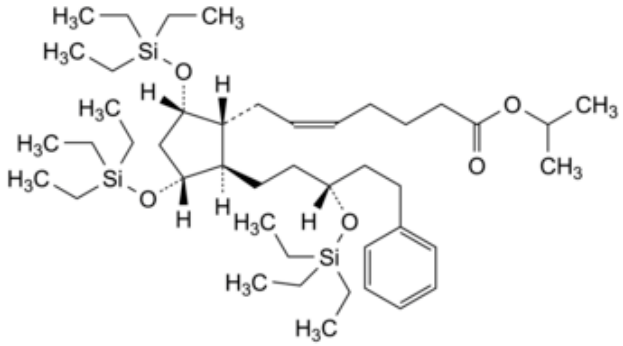
F. propan-2-yl (5*E*)-7-[(1*R*,2*R*,3*R*,5*S*)-3,5-dihydroxy-2-[(3*R*)-3-hydroxy-5-phenylpentyl]cyclopentyl]hept-5-enoate,



G. methyl (5*Z*)-7-[(1*R*,2*R*,3*R*,5*S*)-3,5-dihydroxy-2-[(3*R*)-3-hydroxy-5-phenylpentyl]cyclopentyl]hept-5-enoate,



H. (5*Z*)-7-[(1*R*,2*R*,3*R*,5*S*)-3,5-dihydroxy-2-[(3*R*)-3-hydroxy-5-phenylpentyl]cyclopentyl]hept-5-enoic acid,



J. propan-2-yl (5*Z*)-7-[(1*R*,2*R*,3*R*,5*S*)-2-[(3*R*)-5-phenyl-3-[(triethylsilyl)oxy]pentyl]-3,5-bis[(triethylsilyl)oxy]cyclopentyl]hept-5-enoate.

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