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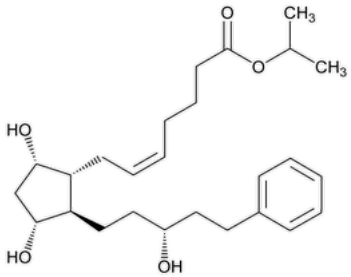
Latanoprost

Change to read:



$C_{26}H_{40}O_5$ ▲432.60▲ (USP 1-Dec-2022)

5-Heptenoic acid, 7-[3,5-dihydroxy-2-(3-hydroxy-5-phenylpentyl)cyclopentyl]-1-methylethyl ester, [1*R*-[1α(*Z*),2β(*R**),3α,5α]]-;
Isopropyl (*Z*)-7-[(1*R*,2*R*,3*R*,5*S*)-3,5-dihydroxy-2-[(3*R*)-3-hydroxy-5-phenylpentyl]cyclopentyl]-5-heptenoate CAS RN®: 130209-82-4; UNII: 6Z5B6HVF6O.

DEFINITION

Latanoprost contains NLT 94.0% and NMT 102.0% of latanoprost ($C_{26}H_{40}O_5$), calculated on the anhydrous and solvent-free basis.

[Caution—Wear protective glasses and gloves while handling the material. Avoid contact during pregnancy or while nursing.]

IDENTIFICATION

Change to read:

• **A.** **Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197F ▲or 197A▲ (USP 1-Dec-2022)

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

Change to read:

• **Procedure**

Mobile phase: Chromatographic hexane and dehydrated alcohol (94:6)

System suitability solution: 2.0 mg/mL of USP Latanoprost RS and 20 µg/mL of USP Latanoprost Related Compound A RS prepared as follows. Transfer USP Latanoprost RS and USP Latanoprost Related Compound A RS into a suitable volumetric flask, dissolve in dehydrated alcohol equivalent to 20% of the final volume, and dilute with chromatographic hexane to volume.

Standard solution: ▲2.0 mg/mL of USP Latanoprost RS prepared as follows. Transfer USP Latanoprost RS into a suitable volumetric flask, dissolve in dehydrated alcohol equivalent to 20% of the final volume, and dilute with chromatographic hexane to volume.▲ (ERR 1-Dec-2022)

Sample solution: ▲2.0 mg/mL of Latanoprost prepared as follows. Transfer Latanoprost into a suitable volumetric flask, dissolve in dehydrated alcohol equivalent to 20% of the final volume, and dilute with chromatographic hexane to volume.▲ (ERR 1-Dec-2022)

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 210 nm

Column: 4.0-mm × 25-cm; 5-µm packing L3

Temperatures

▲Autosampler: 5°▲ (USP 1-Dec-2022)

Column: 30°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[Note—The relative retention times for latanoprost and latanoprost related compound A are 1.0 and 1.1, respectively.]

Suitability requirements

Resolution: NLT 2.0 between latanoprost and latanoprost related compound A, *System suitability solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of latanoprost ($C_{26}H_{40}O_5$) in the portion of Latanoprost taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak area ▲of latanoprost▲ (USP 1-Dec-2022) from the *Sample solution*

r_S = peak area ▲of latanoprost▲ (USP 1-Dec-2022) from the *Standard solution*

C_S = concentration of USP Latanoprost RS in the *Standard solution* (mg/mL)

C_U = concentration of Latanoprost in the *Sample solution* (mg/mL)

Acceptance criteria: 94.0%–102.0% on the anhydrous and solvent-free basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.50%

Change to read:

• **Organic Impurities**

Mobile phase, System suitability solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

▲**Standard stock solution:** 0.3 mg/mL of USP Orlistat Related Compound C RS in a mixture of chromatographic hexane and dehydrated alcohol (80:20) prepared as follows. Transfer USP Orlistat Related Compound C RS into a suitable volumetric flask, dissolve in dehydrated alcohol equivalent to 20% of the final volume, and dilute with chromatographic hexane to volume.▲ (USP 1-Dec-2022)

Standard solution: 0.04 mg/mL of USP Latanoprost RS ▲and 0.003 mg/mL of USP Orlistat Related Compound C RS▲ (USP 1-Dec-2022) in a mixture of chromatographic hexane and dehydrated alcohol (80:20) prepared as follows. Transfer USP Latanoprost RS into a suitable volumetric flask, dissolve in dehydrated alcohol equivalent to 20% of the final volume, ▲add a suitable amount of the *Standard stock solution*,▲ (USP 1-Dec-2022) and dilute with chromatographic hexane to volume.

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between latanoprost and latanoprost related compound A, *System suitability solution*

Relative standard deviation: NMT 5.0% ▲for latanoprost and orlistat related compound C,▲ (USP 1-Dec-2022) *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

▲Calculate the percentage of orlistat related compound C in the portion of Latanoprost taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak area of orlistat related compound C from the *Sample solution*

r_S = peak area of orlistat related compound C from the *Standard solution*

C_S = concentration of USP Orlistat Related Compound C RS in the *Standard solution* (mg/mL)

C_U = concentration of Latanoprost in the *Sample solution* (mg/mL)▲ (USP 1-Dec-2022)

Calculate the percentage of ▲any other▲ (USP 1-Dec-2022) impurity in the portion of Latanoprost taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak area of ▲any other▲ (USP 1-Dec-2022) impurity from the *Sample solution*

r_S = peak area of latanoprost from the *Standard solution*

C_S = concentration of USP Latanoprost RS in the *Standard solution* (mg/mL)

C_U = concentration of Latanoprost in the *Sample solution* (mg/mL)

F = relative response factor for each individual impurity (see *Table 1*)

Acceptance criteria: See *Table 1*. ▲The reporting threshold is▲ (USP 1-Dec-2022) 0.05%.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
▲Orlistat related compound C	0.67	—	0.15▲ (USP 1-Dec-2022)
Isopropyl diphenylphosphorylpentanoate[a]	0.79	2.4	0.1
Latanoprost related compound B[b]	0.89	1.0	0.5
Latanoprost	1.00	—	—
Latanoprost related compound A▲▲ (USP 1-Dec-2022)	1.10	1.0	3.5
Any unspecified impurity	—	1.0	0.1
Total impurities[c]	—	—	0.5

[a] Isopropyl 5-(diphenylphosphoryl)pentanoate.

[b] Isopropyl (*Z*)-7-[(1*R*,2*R*,3*R*,5*S*)-3,5-dihydroxy-2-[(3*S*)-3-hydroxy-5-phenylpentyl]cyclopentyl]-5-heptenoate.

[c] Latanoprost related compound A and latanoprost related compound B are excluded.

- **Limit of Latanoprost Related Compound E**

Solution A: Acetonitrile, phosphoric acid, and water (300:1:700)

Solution B: Acetonitrile, phosphoric acid, and water (800:1:200)

Mobile phase: See *Table 2*.

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	100	0
9	100	0
10	0	100
15	0	100
16	100	0
21	100	0

Diluent: Acetonitrile and water (30:70)

Standard solution: 1.0 µg/mL of USP Latanoprost Related Compound E RS in *Diluent*

Sample solution: 1.0 mg/mL of Latanoprost in *Diluent*

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 200 nm

Column: 4.0-mm × 15-cm; 5-µm packing L1

Column temperature: 60°

Flow rate: 1.0 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 5.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of latanoprost related compound E in the portion of Latanoprost taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak area of latanoprost related compound E from the *Sample solution*

r_S = peak area of latanoprost related compound E from the *Standard solution*

C_S = concentration of USP Latanoprost Related Compound E RS in the *Standard solution* (mg/mL)

C_U = concentration of Latanoprost in the *Sample solution* (mg/mL)

Acceptance criteria: NMT 0.2%

SPECIFIC TESTS

• **Optical Rotation** ⟨781S⟩, *Procedures, Specific Rotation*

Sample solution: 10 mg/mL of Latanoprost in acetonitrile

Acceptance criteria: +31° to +38°

Change to read:

• **Water Determination** ⟨921⟩, *Method I, Method Ic,* ▲or *Method Ia*▲ (USP 1-Dec-2022)

Sample solution: 100 mg/mL of Latanoprost in ethyl acetate▲▲ (USP 1-Dec-2022)

Acceptance criteria: NMT 2.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed, light-resistant containers, and store in a refrigerator or a freezer.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Latanoprost RS

USP Latanoprost Related Compound A RS

Isopropyl (*E*)-7-{(1*R*,2*R*,3*R*,5*S*)-3,5-dihydroxy-2-[(3*R*)-3-hydroxy-5-phenylpentyl]cyclopentyl}-5-heptenoate.

$C_{26}H_{40}O_5$ 432.59

USP Latanoprost Related Compound E RS

(*Z*)-7-{(1*R*,2*R*,3*R*,5*S*)-3,5-Dihydroxy-2-[(*R*)-3-hydroxy-5-phenylpentyl]cyclopentyl}-5-heptenoic acid.

$C_{23}H_{34}O_5$ 390.51

▲USP Orlistat Related Compound C RS

Triphenyl phosphine oxide

$C_{18}H_{15}OP$ 278.28▲ (USP 1-Dec-2022)

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
LATANOPROST	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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