Latanoprost Eye Drops

Details for the public consultation of this monograph are as follows:

EAG/Panel/Working Party	Medicinal Chemicals 2
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Notes	**New monograph** If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required.

Action and use

Prostaglandin (PGF_{2a}) analogue; treatment of intraocular pressure.

DEFINITION

Latanoprost Eye Drops are a sterile solution of Latanoprost in a suitable vehicle.

The eye drops comply with the requirements stated under Eye Preparations and with the following requirements.

Content of latanoprost, $C_{26}H_{40}O_5$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

In the Assay, record the UV spectrum of the principal peak in the chromatograms obtained with solutions (1) and (2) with a diode array detector in the range of 190 to 400 nm.

The UV spectrum of the principal peak in the chromatogram obtained with solution (1) is similar to that of the peak in the chromatogram obtained with solution (2);
the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the peak in the chromatogram obtained with solution (2).

TESTS

Acidity or alkalinity

pH of a 0.005% w/v solution, 5.8 to 7.5, Appendix V L.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions. *Prepare the solutions immediately before use and protect from light.*

(1) Dilute a volume of the eye drops with mobile phase A, if necessary, to produce a solution containing 0.005% w/v of Latanoprost.
(2) Dilute 1 volume of solution (1) to 100 volumes with mobile phase A.
(3) 0.00005% w/v of *latanoprost impurity standard BPCRS* (containing impurities H and F) in mobile phase A.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *base-deactivated end-capped octadecylsilyl silica gel* (3 µm) (ACE C18 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use a column temperature of 35°.

(e) Use a detection wavelength of 208 nm.
(f) Inject 100 µL of each solution.

MOBILE PHASE

Mobile phase A 40 volumes of *acetonitrile R1* and 60 volumes of a 0.34% w/v solution of *potassium dihydrogen orthophosphate* previously adjusted to pH 3.0 with *orthophosphoric acid*.

Mobile phase B *acetonitrile R1*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-50	100	0	isocratic
50-60	100→75	0→25	linear gradient
60-70	75	25	isocratic
70-70.1	75→100	25→0	linear gradient
70.1-82	100	0	re-equilibration

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to latanoprost and impurity F is at least 2.0.

CALCULATION OF IMPURITIES

For all impurities, use the concentration of Latanoprost in solution (2).

Latanoprost retention time: about 29 minutes.

Relative retention: impurity H, about 0.2; and impurity F; about 1.04.

LIMITS

Impurity F: 4.0%.

Impurity H: 1.5%.

Individual unspecified impurities: 1.0%.

Total impurities, excluding impurity F: 3.0%.

Reporting threshold: 0.1%.

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Dilute a volume of the eye drops with mobile phase A, if necessary, to produce a solution containing 0.005% w/v of Latanoprost.
(2) 0.005% w/v of *latanoprost BPCRS* in mobile phase A.
(3) 0.005% w/v of *latanoprost impurity standard BPCRS* (containing impurities H and F) in mobile phase A.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *base-deactivated end-capped octadecylsilyl silica gel* (3 µm) (ACE C18 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use a column temperature of 35°.
(e) Use a detection wavelength of 208 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

Mobile phase A 40 volumes of *acetonitrile R1* and 60 volumes of a 0.34% w/v solution of *potassium dihydrogen orthophosphate* previously adjusted to pH 3.0 with *orthophosphoric acid*.

Mobile phase B *acetonitrile R1*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-7	100	0	isocratic
7-7.1	100→75	0→25	linear gradient
7.1-12	75	25	isocratic
12-12.1	75→100	25→0	linear gradient
12.1-22	100	0	re-equilibration

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to latanoprost and impurity F is at least 2.0.

Latanoprost retention time: about 5 minutes.

DETERMINATION OF CONTENT

Calculate the content of $C_{26}H_{40}O_5$, in the eye drops from the chromatograms obtained and using the declared content of $C_{26}H_{40}O_5$, in *latanoprost BPCRS*.

STORAGE

Latanoprost Eye Drops should be kept in an airtight container and protected from light.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities F and H listed under *Latanoprost*.