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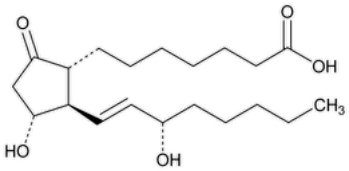
Alprostadil



$C_{20}H_{34}O_5$ 354.48

Prost-13-en-1-oic acid, 11,15-dihydroxy-9-oxo-, (11α,13*E*,15*S*)-;

(1*R*,2*R*,3*R*)-3-Hydroxy-2-[(*E*)-(3*S*)-3-hydroxy-1-octenyl]-5- oxocyclopentaneheptanoic acid CAS RN®: 745-65-3; UNII: F5TD010360.

DEFINITION

Alprostadil contains NLT 95.0% and NMT 105.0% of alprostadil ($C_{20}H_{34}O_5$), calculated on the anhydrous basis.

[**Caution—**Great care should be taken to prevent inhaling particles of Alprostadil and exposing the skin to it.]

IDENTIFICATION

Change to read:

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

ASSAY

• **Procedure**

Use freshly prepared solutions.

Mobile phase: Methanol, acetonitrile, and 0.1 M monobasic potassium phosphate (2:1:2). Adjust with phosphoric acid to a pH of 3.0.

Diluent: Methanol and water (90:10)

Internal standard solution: 0.05 mg/mL of ethylparaben in *Diluent*

Standard stock solution: 0.3 mg/mL of USP Alprostadil RS in *Diluent*

Standard solution: 0.2 mg/mL of USP Alprostadil RS prepared by combining 2.0 mL of *Standard stock solution* with 1.0 mL of *Internal standard solution*

System suitability stock solution: 4.5 µg/mL of USP Prostaglandin A1 RS in *Standard stock solution*

System suitability solution: Combine 2.0 mL of *System suitability stock solution* with 1.0 mL of *Internal standard solution.*

Sample stock solution: 0.3 mg/mL of Alprostadil in *Diluent*

Sample solution: 0.2 mg/mL of Alprostadil prepared by combining 2.0 mL of *Sample stock solution* and 1.0 mL of *Internal standard solution*

Chromatographic system

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

Mode: LC

Detector: Photodiode array detector or equivalent capable of detecting UV wavelengths of 200–300 nm

Analytical wavelength: 200 nm

Column: 4.6-mm × 25-cm; packing L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 7.5 between prostaglandin A_1 and alprostadil, and NLT 2.0 between prostaglandin A_1 and ethylparaben

Relative standard deviation: NMT 2.0%, determined from the peak area ratio of alprostadil to ethylparaben

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of alprostadil ($C_{20}H_{34}O_5$) in the portion of Alprostadil taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = peak area ratio of alprostadil to the internal standard from the *Sample solution*

R_S = peak area ratio of alprostadil to the internal standard from the *Standard solution*

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

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

Acceptance criteria: 95.0%–105.0% on the anhydrous basis

IMPURITIES

• **Residue on Ignition ⟨281⟩**

Sample: 0.3 g

Acceptance criteria: NMT 0.5%

Delete the following:

▲• **Limit of Chromium**

Standard stock solution: 3.04 µg/mL of chromium trichloride in 0.05 M nitric acid

Standard solution: 20 ng/mL of chromium (Cr) in alcohol, prepared as follows. Transfer 2 mL of the *Standard stock solution* to a 100-mL volumetric flask, and dilute with alcohol to volume.

Sample solution: 1.0 mg/mL of Alprostadil in alcohol

Blank: Alcohol

Instrumental conditions

(See *Atomic Absorption Spectroscopy ⟨852⟩*.)

Mode: Atomic absorption spectroscopy

Lamp: Chromium hollow-cathode

Analytical wavelength: 357.9 nm

Atomization type: Graphite furnace

Temperatures

Drying: 100°

Ashing: 1000°

Atomization: 2700°

Injection volume: 20 µL

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of chromium (Cr) in the portion of Alprostadil taken:

$$\text{Result} = (A_U/A_S) \times (C_S/C_U) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of chromium in the *Standard solution* (mg/mL)

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

Acceptance criteria: NMT 0.002%▲ (USP 1-May-2022)

Delete the following:

▲• **Limit of Rhodium**

Standard stock solution: 100 µg/mL of rhodium in 1.2 M hydrochloric acid, prepared by diluting rhodium chloride hydrate

Standard solution: 50 ng/mL of rhodium (Rh) in alcohol from *Standard stock solution*

Sample solution: 2.0 mg/mL of Alprostadil in alcohol

Blank: Alcohol

Instrumental conditions

(See *Atomic Absorption Spectroscopy ⟨852⟩*.)

Mode: Atomic absorption spectroscopy

Lamp: Rhodium hollow-cathode

Analytical wavelength: 343.5 nm

Atomization type: Graphite furnace

Temperatures

Drying: 100°

Ashing: 1000°

Atomization: 2800°

Injection volume: 20 µL

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of rhodium (Rh) in the portion of Alprostadil taken:

$$\text{Result} = (A_U/A_S) \times (C_S/C_U) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of rhodium in the *Standard solution* (mg/mL)

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

Acceptance criteria: NMT 0.002%▲ (USP 1-May-2022)

Change to read:

• **Limit of Foreign Prostaglandins, Test 1**

Use freshly prepared solutions.

Mobile phase: Methanol, acetonitrile, and 0.1 M monobasic potassium phosphate (2:1:2). Adjust with phosphoric acid to a pH of 3.0.

Diluent: Methanol and water (90:10)

Standard solution: 6 µg/mL of USP Alprostadil RS, 15 µg/mL of USP Prostaglandin A1 RS, and 6 µg/mL of USP Prostaglandin B1 RS in *Diluent*

Sample solution: 3.0 mg/mL of Alprostadil in *Diluent*

Chromatographic system

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

Mode: LC

Detector: Photodiode array detector or equivalent capable of detecting UV wavelengths of 200–300 nm

Analytical wavelengths

Prostaglandin A_1: 224 nm

Prostaglandin B_1: 280 nm

Other foreign prostaglandins: 200 nm

Column: 4.6-mm × 25-cm; packing L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 7.5 between prostaglandin A_1 and alprostadil

Relative standard deviation: NMT 4.0%, determined from the peaks at their respective wavelength for replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of prostaglandin A_1 and prostaglandin B_1 in the portion of Alprostadil taken:

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

r_U = peak response of prostaglandin A_1 or prostaglandin B_1 from the *Sample solution*

r_S = peak response of prostaglandin A_1 or prostaglandin B_1 from the *Standard solution*

C_S = concentration of USP Prostaglandin A1 RS or USP Prostaglandin B1 RS in the *Standard solution* (mg/mL)

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

Calculate the percentage of each impurity occurring at 200 nm and eluting before prostaglandin A_1 in the portion of Alprostadil taken:

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

r_U = peak response for each impurity from the *Sample solution*

r_S = peak response for alprostadil from the *Standard solution*

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

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

Calculate the percentage of ▲any▲ (USP 1-May-2022) impurity having a relative retention time of 0.6, relative to the prostaglandin A_1 peak detected at 224 nm, in the portion of Alprostadil taken:

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

r_U = peak response for any impurity having a relative retention time of 0.6, relative to the prostaglandin A_1 peak, from the *Sample solution*

r_S = peak response for prostaglandin A_1 from the *Standard solution*

C_S = concentration of USP Prostaglandin A1 RS in the *Standard solution* (mg/mL)

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

Acceptance criteria

Prostaglandin A_1: NMT 1.5%

Prostaglandin B_1: NMT 0.1%

Any foreign prostaglandin impurity eluting before prostaglandin A_1: NMT 0.9%

Impurity at relative retention time 0.6, relative to prostaglandin A_1: NMT 0.9%

Change to read:

• **Limit of Foreign Prostaglandins, Test 2**

Mobile phase: Methanol, acetonitrile, and 0.02 M monobasic potassium phosphate (2:1:1). Adjust with phosphoric acid to a pH of 3.

System suitability solution: 6 µg/mL of USP Alprostadil RS, 15 µg/mL of USP Prostaglandin A1 RS, and 6 µg/mL of USP Prostaglandin B1 RS in methanol and water (9:1)

Standard solution: 10 µg/mL of USP Alprostadil RS in acetonitrile and water (1:1)

Sample solution: 5.0 mg/mL of Alprostadil in acetonitrile and water (1:1). [Note—Sonicate if necessary.]

Chromatographic system

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

Mode: LC

Detector: Photodiode array detector or equivalent, capable of detecting UV wavelengths of 200–300 nm

Analytical wavelengths

Prostaglandin A_1: 224 nm

Prostaglandin B_1: 280 nm

Other foreign prostaglandins: 200 nm

Column: 4.6-mm × 25-cm; packing L1

Flow rate: 1.2 mL/min

Injection volume: 20 µL

System suitability

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

[Note—The relative retention times for alprostadil and prostaglandin A_1 are 1.0 and 1.2, respectively. ▲(USP 1-May-2022)]

Suitability requirements

Resolution: NLT 4.0 between prostaglandin A_1 and alprostadil, *System suitability solution*

Relative standard deviation: NMT 2.0%, determined from the main peak, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity, excluding prostaglandin B_1, observed at 200 nm and eluting after prostaglandin A_1 in the portion of Alprostadil taken:

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

r_U = peak response for each impurity from the *Sample solution*

r_S = peak response for alprostadil from the *Standard solution*

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

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

Acceptance criteria

Sum of the impurities at relative retention times 2.0 and 2.3: NMT 0.6%

Any other foreign prostaglandin impurity eluting after prostaglandin A_1: NMT 0.9%

Total impurities: The sum of the impurities from *Limit of Foreign Prostaglandins, Test 1* and *Test 2*, is NMT 2.0%.

SPECIFIC TESTS

• **Water Determination** ⟨921⟩, *Method I*

Sample: 0.5 g

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store in a refrigerator.

• **USP Reference Standards** ⟨11⟩

USP Alprostadil RS

USP Prostaglandin A1 RS

USP Prostaglandin B1 RS

(13*E*,15*S*)-15-Hydroxy-9-oxoprosta-8(12),13-dien-1-oic acid.

$C_{20}H_{32}O_4$ 336.47

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

Topic/Question	Contact	Expert Committee
ALPROSTADIL	Documentary Standards Support	SM52020 Small Molecules 5
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 46(5)

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