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Prilocaine and Epinephrine Injection

DEFINITION

Prilocaine and Epinephrine Injection is a sterile solution prepared from Prilocaine Hydrochloride and Epinephrine with the aid of Hydrochloric Acid in Water for Injection, or a sterile solution of Prilocaine Hydrochloride and Epinephrine Bitartrate in Water for Injection. The content of epinephrine does not exceed 0.002% (1 in 50,000). Prilocaine and Epinephrine Injection contains the equivalent of NLT 95.0% and NMT 105.0% of the labeled amount of prilocaine hydrochloride ($C_{13}H_{20}N_2O \cdot HCl$) and the equivalent of NLT 90.0% and NMT 115.0% of the labeled amount of epinephrine ($C_9H_{13}NO_3$).

IDENTIFICATION

• **A.**

Sample: A volume of Injection equivalent to 300 mg of prilocaine hydrochloride

Analysis: Dilute the *Sample* with 5 mL of water, and add 4 mL of 6 N ammonium hydroxide. Extract with 50 mL of chloroform, and filter the extract. Evaporate the filtrate on a steam bath with the aid of a current of air. Dissolve 100 mg of the prilocaine so obtained in 1 mL of alcohol, add 10 drops of cobaltous chloride TS, and shake for 2 min.

Acceptance criteria: A bright green color develops, and a precipitate is formed.

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

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

ASSAY

• **Prilocaine Hydrochloride**

Solution A: 50 mL of glacial acetic acid in 930 mL of water. Adjust with 1 N sodium hydroxide to a pH of 3.40.

Mobile phase: Acetonitrile and *Solution A* (1:4). Adjust the ratio of the mobile phase components to obtain a retention time of 4–6 min for the prilocaine peak. Pass through a membrane filter of 1-µm or finer pore size, and degas.

Standard solution: 4 mg/mL of USP Prilocaine Hydrochloride RS in *Mobile phase*

System suitability stock solution: 900 µg/mL of procainamide hydrochloride in *Mobile phase*

System suitability solution: *System suitability stock solution* and *Standard solution* (1:10)

Sample solution: Nominally 4 mg/mL of prilocaine hydrochloride from Injection, in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 30-cm; packing L1

Column temperature: 20°–25°, maintained at ±1.0° of the selected temperature

Flow rate: 1.5 mL/min

Injection volume: 10 µL

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between prilocaine and procainamide, *System suitability solution*

Relative standard deviation: NMT 1.5%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of prilocaine hydrochloride ($C_{13}H_{20}N_2O \cdot HCl$) in the volume of Injection taken:

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

r_U = peak area of prilocaine hydrochloride from the *Sample solution*

r_S = peak area of prilocaine hydrochloride from the *Standard solution*

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

C_U = nominal concentration of prilocaine hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 95.0%–105.0%

- **Epinephrine**

Solution A: Mix 50 mL of glacial acetic acid and 930 mL of water, and adjust with 1 N sodium hydroxide to a pH of 3.40. Dissolve 1.1 g of sodium 1-heptanesulfonate in this solution, and add 1.0 mL of 0.1 M disodium ethylenediaminetetraacetate.

Mobile phase: Methanol and *Solution A* (1:9). Pass through a membrane filter of 1-µm or finer pore size, and degas.

Standard solution: 1.8 µg/mL of USP Epinephrine Bitartrate RS in *Mobile phase*

Sample solution: Nominally 1 µg/mL of epinephrine from Injection in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: An electrochemical detector held at a potential of +650 mV, and a controller capable of regulating the background current

Column: 3.9-mm × 30-cm; packing L1

Column temperature: 20°–25°, maintained at ±1.0° of the selected temperature

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 1.5%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of epinephrine ($C_9H_{13}NO_3$) in the volume of Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of epinephrine from the *Sample solution*

r_S = peak response of epinephrine from the *Standard solution*

C_S = concentration of USP Epinephrine Bitartrate RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of epinephrine in the *Sample solution* (µg/mL)

M_{r1} = molecular weight of epinephrine, 183.20

M_{r2} = molecular weight of epinephrine bitartrate, 333.29

Acceptance criteria: 90.0%–115.0%

SPECIFIC TESTS

- **Color and Clarity**

Standard solution: Transfer 2.0 mL of 0.100 N iodine VS to a 500-mL volumetric flask, and dilute with water to volume.

Sample solution: A portion of the Injection

Analysis

Samples: *Standard solution* and *Sample solution*

Visually examine the *Sample solution* in a suitable clear glass test tube against a white background: it is not pinkish, and it contains no precipitate. If any yellow color is observed in the *Sample solution*, concomitantly determine the absorbances of the *Sample solution* and the *Standard solution* in 1-cm cells with a suitable spectrophotometer set at 460 nm.

Acceptance criteria: The absorbance of the *Sample solution* does not exceed that of the *Standard solution*.

- **Bacterial Endotoxins Test ⟨85⟩:** It contains NMT 0.9 USP Endotoxin Unit/mg of prilocaine hydrochloride.

• **pH ⟨791⟩:** 3.3–5.5

• **Other Requirements:** It meets the requirements in *Injections and Implanted Drug Products ⟨1⟩*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in single-dose or multiple-dose light-resistant containers, preferably of Type I glass.

• **Labeling:** The label indicates that the Injection is not to be used if its color is pinkish or darker than slightly yellow or if it contains a precipitate.

• **USP Reference Standards ⟨11⟩**

USP Epinephrine Bitartrate RS

USP Prilocaine Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
PRILOCAINE AND EPINEPHRINE INJECTION	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

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