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Mepivacaine Hydrochloride and Levonordefrin Injection

DEFINITION

Mepivacaine Hydrochloride and Levonordefrin Injection is a sterile solution of Mepivacaine Hydrochloride and Levonordefrin in Water for Injection. It contains NLT 95.0% and NMT 105.0% of the labeled amount of mepivacaine hydrochloride ($C_{15}H_{22}N_2O \cdot HCl$) and NLT 90.0% and NMT 110.0% of the labeled amount of levonordefrin ($C_9H_{13}NO_3$).

IDENTIFICATION

- **A.**

Analysis: Extract a volume of Injection, equivalent to 200 mg of mepivacaine, with two 10-mL portions of ether, and discard the ether extracts. Render slightly alkaline with sodium carbonate TS, extract the precipitate with ether, evaporate the ether extract on a steam bath to dryness, and dry the residue under vacuum at 60° for 1 h.

Acceptance criteria: The mepivacaine obtained melts between 149° and 153°.

- **B. Identification Tests—General, *Chloride* ⟨191⟩:** Meets the requirements

ASSAY

- **Mepivacaine Hydrochloride**

Buffer: 3.40 g/L of monobasic potassium phosphate and 4.35 g/L of dibasic potassium phosphate in water. Adjust with potassium hydroxide or phosphoric acid to a pH of 6.3.

Mobile phase: Acetonitrile and *Buffer* (35:65)

System suitability solution: 0.05 mg/mL of methylparaben and 1.0 mg/mL of USP Mepivacaine Hydrochloride RS in *Mobile phase*

Standard solution: 1.0 mg/mL of USP Mepivacaine Hydrochloride RS in *Mobile phase*

Sample solution: Nominally 1 mg/mL of mepivacaine hydrochloride from Injection in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 263 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1[1]

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

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

[Note—The relative retention times for mepivacaine and methylparaben are 1.0 and 1.4, respectively.]

Suitability requirements

Resolution: NLT 2.0 between methylparaben and mepivacaine, *System suitability solution*

Capacity factor: NLT 1.0 for the mepivacaine peak, *System suitability solution*

Tailing factor: NMT 2.0 for the mepivacaine peak, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of mepivacaine hydrochloride ($C_{15}H_{22}N_2O \cdot HCl$) in the volume of Injection taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

Acceptance criteria: 95.0%–105.0%

- **Levonordefrin**

Ferro-citrate solution and **Buffer solution:** Prepare as directed in *Epinephrine Assay* ⟨391⟩.

Standard stock solution: With the aid of 20 mL of sodium bisulfite solution (1 in 50), transfer 25 mg of USP Levonordefrin RS to a 50-mL volumetric flask, and dilute with water to volume.

Standard solution: 50 µg/mL of USP Levonordefrin RS in sodium bisulfite solution (1 in 500) from the *Standard stock solution*. Make the final dilution at the time the *Assay* is to be carried out.

Sample solution: Nominally 50 µg/mL of levonordefrin from Injection, diluting if necessary

Analysis: Proceed as directed in *Epinephrine Assay* ⟨391⟩, except use levonordefrin wherever epinephrine [base] is called for. When the *Ferro-citrate solution* and the *Buffer solution* are mixed with the *Sample solution*, a fine precipitate may be formed. Remove this precipitate by centrifugation or by passing through dry filter paper before the colorimetric measurements are taken.

Calculate the percentage of the labeled amount of levonordefrin ($C_9H_{13}NO_3$) in the volume of Injection 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 USP Levonordefrin RS in the *Standard solution* (µg/mL)

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

Acceptance criteria: 90.0%–110.0%

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.

Analysis

Samples: *Standard solution* and *Sample solution*

Visually examine a portion of the Injection (*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 *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*.

- **pH** ⟨791⟩ **:** 3.3–5.5
- **Bacterial Endotoxins Test** ⟨85⟩ **:** It contains NMT 0.8 USP Endotoxin Unit/mg of mepivacaine hydrochloride.
- **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 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 Levonordefrin RS

USP Mepivacaine Hydrochloride RS

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1 A Whatman Partisphere RTF C18 brand of L1 column has been shown to be an appropriate column.

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

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