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Lidocaine Hydrochloride and Epinephrine Injection

» Lidocaine Hydrochloride and Epinephrine Injection is a sterile solution prepared from Lidocaine Hydrochloride and Epinephrine with the aid of Hydrochloric Acid in Water for Injection, or a sterile solution prepared from Lidocaine and Epinephrine with the aid of Hydrochloric Acid in Water for Injection, or a sterile solution of Lidocaine Hydrochloride and Epinephrine Bitartrate in Water for Injection. The content of epinephrine does not exceed 0.002 percent (1 in 50,000). Lidocaine Hydrochloride and Epinephrine Injection contains the equivalent of not less than 95.0 percent and not more than 105.0 percent of the labeled amount of lidocaine hydrochloride ($C_{14}H_{22}N_2O \cdot HCl$) and the equivalent of not less than 90.0 percent and not more than 115.0 percent of the labeled amount of epinephrine ($C_9H_{13}NO_3$).

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 Lidocaine RS

Color and clarity—Using the Injection as the *Test solution*, proceed as directed for *Color and clarity* under *Epinephrine Injection*.

Bacterial Endotoxins Test ⟨85⟩ —It contains not more than 0.7 USP Endotoxin Unit per mg of lidocaine hydrochloride.

pH ⟨791⟩: between 3.3 and 5.5.

Other requirements—It responds to the *Identification* test under *Lidocaine Hydrochloride Injection*. It meets also the requirements under *Injections and Implanted Drug Products ⟨1⟩*.

Assay for lidocaine hydrochloride—

Mobile phase—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. Mix about 4 volumes of this solution with 1 volume of acetonitrile, so that the retention time of lidocaine is about 4 to 6 minutes. Pass through a membrane filter having a 1-µm or finer porosity, and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Standard preparation—Dissolve about 85 mg of USP Lidocaine RS, accurately weighed, with warming if necessary, in 0.5 mL of 1 N hydrochloric acid in a 50-mL volumetric flask, dilute with *Mobile phase* to volume, and mix to obtain a *Standard preparation* having a known concentration of about 1.7 mg of lidocaine per mL.

Assay preparation—Transfer an accurately measured volume of Injection, equivalent to about 100 mg of lidocaine hydrochloride, to a 50-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Resolution preparation—Prepare a solution of methylparaben in *Mobile phase* containing about 220 µg per mL. Mix 2 mL of this solution and 20 mL of the *Standard preparation*.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 254-nm detector and a 3.9-mm × 30-cm column that contains packing L1. The flow rate is about 1.5 mL per minute. Chromatograph about 20 µL of the *Resolution preparation,* and record the peak responses as directed for *Procedure:* the resolution, *R,* between lidocaine and methylparaben is not less than 3.0. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 1.5%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Assay preparation* and the *Standard preparation* into the chromatograph. Record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of lidocaine hydrochloride ($C_{14}H_{22}N_2O \cdot HCl$) in each mL of the Injection taken by the formula:

$$(270.80/234.34)(50)(C/V)(r_U/r_S)$$

in which 270.80 and 234.34 are the molecular weights of lidocaine hydrochloride and lidocaine, respectively; C is the concentration, in mg per mL, of USP Lidocaine RS in the *Standard preparation; V* is the volume, in mL, of Injection taken; and r_U and r_S are the lidocaine peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Assay for epinephrine—

Mobile phase—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, add 1.0 mL of 0.1 M edetate disodium, and mix. Mix about 9 volumes of this solution with 1 volume of methanol, so that the retention time of epinephrine is about 4 to 6 minutes. Pass through a membrane filter having a 1-µm or finer porosity, and degas.

Standard preparation—Dissolve an accurately weighed quantity of USP Epinephrine Bitartrate RS in *Mobile phase* to obtain a solution having a known concentration of about 9 µg of epinephrine bitartrate per mL. Pipet 10 mL of this solution into a 50-mL volumetric flask, dilute with *Mobile phase* to volume, and mix to obtain a *Standard preparation* having a known concentration of about 1.8 µg of epinephrine bitartrate per mL.

Assay preparation—Transfer an accurately measured volume of Injection, equivalent to about 50 µg of epinephrine, to a 50-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is fitted with a 3.9-mm × 30-cm stainless steel column that contains packing L1 and is equipped with an electrochemical detector held at a potential of +650 mV, a controller capable of regulating the background current, and a suitable recorder. The flow rate is about 1 mL per minute. Chromatograph the *Standard preparation* as directed for *Procedure:* the relative standard deviation of the peak responses of successive injections of the *Standard preparation* is not more than 1.5%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Assay preparation* and the *Standard preparation* into the chromatograph by means of a suitable microsyringe or sampling valve, adjusting the specimen size and other operating parameters so that satisfactory chromatography and peak responses are obtained. Record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in µg, of epinephrine ($C_9H_{13}NO_3$) in each mL of the Injection taken by the formula:

$$(183.20/333.29)(50)(C/V)(r_U/r_S)$$

in which 183.20 and 333.29 are the molecular weights of epinephrine and epinephrine bitartrate, respectively; C is the concentration, in µg per mL, of USP Epinephrine Bitartrate RS in the *Standard preparation; V* is the volume, in mL, of Injection taken; and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

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

Topic/Question	Contact	Expert Committee
LIDOCAINE HYDROCHLORIDE 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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