Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-May-2018
Document Type: USP Monographs
DocId: GUID-41D1AE31-D0A4-4424-940B-D2B764F1CE3A_3_en-US
DOI: https://doi.org/10.31003/USPNF_M57330_03_01
DOI Ref: qh0tu

Norepinephrine Bitartrate Injection

» Norepinephrine Bitartrate Injection is a sterile solution of Norepinephrine Bitartrate in Water for Injection. It contains the equivalent of not less than 90.0 percent and not more than 115.0 percent of the labeled amount of norepinephrine ($C_8H_{11}NO_3$).

Packaging and storage—Preserve in single-dose, light-resistant containers, preferably of Type I glass.

Labeling—Label the Injection in terms of mg of norepinephrine per mL, and, where necessary, label it to indicate that it must be diluted prior to use. 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 Norepinephrine Bitartrate RS

Color and clarity—

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

Procedure—Visually examine a portion of the Injection *(Test 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 *Test solution*, concomitantly determine the absorbances of the *Test solution* and the *Standard solution* in 1-cm cells with a suitable spectrophotometer set at 460 nm: the absorbance of the *Test solution* does not exceed that of the *Standard solution.*

Identification—

A: It responds to *Identification* test *B* under *Norepinephrine Bitartrate*.

B: Dilute the Injection with water to a concentration of 1 mg in 5 mL. To 10 mL of the dilution add 2.0 mL of 0.10 N iodine, allow to stand for 5 minutes, then add 3.0 mL of 0.10 N sodium thiosulfate: the solution is colorless or has at most a slight pink or slight violet color (*epinephrine and isoproterenol at the same pH, about 3.5, give a red-brown or violet color*).

Bacterial Endotoxins Test ⟨85⟩ —It contains not more than 83.4 USP Endotoxin Units per mg of norepinephrine.

pH ⟨791⟩: between 3.0 and 4.5.

Particulate Matter in Injections ⟨788⟩: meets the requirements for small-volume injections.

Other requirements—It meets the requirements under *Injections and Implanted Drug Products ⟨1⟩*.

Assay—

Mobile phase—Dissolve 1.1 g of sodium 1-heptanesulfonate in 800 mL of water. Add 200 mL of methanol, and adjust with 1 M phosphoric acid to a pH of 3.0 ± 0.1. Pass through a membrane filter. Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Standard preparation—Dissolve an accurately weighed quantity of USP Norepinephrine Bitartrate RS in freshly prepared dilute acetic acid (1 in 25), and dilute quantitatively, and stepwise if necessary, to obtain a solution having a known concentration of about 0.4 mg of norepinephrine bitartrate monohydrate per mL.

Assay preparation—Transfer an accurately measured volume of Injection, equivalent to about 5 mg of norepinephrine, to a 25-mL volumetric flask, add dilute acetic acid (1 in 25) to volume, and mix.

System suitability preparation—Dissolve a suitable quantity of isoproterenol hydrochloride in the *Standard preparation* to obtain a solution containing, in each mL, 0.4 mg of USP Norepinephrine Bitartrate RS and 0.4 mg of isoproterenol hydrochloride.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 280-nm detector and a 4.6-mm × 25-cm column that contains packing L1. The flow rate is about 2 mL per minute. Chromatograph the *Standard preparation* and the *System suitability preparation*, and record the peak responses as directed under *Procedure:* the tailing factor for the analyte peak is not more than 2.5, the resolution, *R,* between the norepinephrine and isoproterenol peaks is not less than 4.0, and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of norepinephrine ($C_8H_{11}NO_3$) in each mL of the Injection taken by the formula:

$$(169.18/337.29)(25C/V)(r_U/r_S)$$

in which 169.18 and 337.29 are the molecular weights of norepinephrine and norepinephrine bitartrate monohydrate, respectively; *C* is the concentration, in mg per mL, of USP Norepinephrine 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
NOREPINEPHRINE BITARTRATE INJECTION	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 50(2)

Current DocID: GUID-41D1AE31-D0A4-4424-940B-D2B764F1CE3A_3_en-US
Previous DocID: GUID-41D1AE31-D0A4-4424-940B-D2B764F1CE3A_1_en-US
DOI: https://doi.org/10.31003/USPNF_M57330_03_01
DOI ref: qh0tu