Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-Apr-2023
Document Type: USP Monographs
DocId: GUID-4007C238-514A-47F6-B493-2363E7AFC1D8_5_en-US
DOI: https://doi.org/10.31003/USPNF_M34550_05_01
DOI Ref: 99xzb

Furosemide Injection

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click www.uspnf.com/rb-furosemide-inj-20230331.

DEFINITION

Furosemide Injection is a sterile solution of Furosemide in Water for Injection prepared with the aid of Sodium Hydroxide or, where intended solely for veterinary use, Diethanolamine or Monoethanolamine. It contains NLT 90.0% and NMT 110.0% of the labeled amount of furosemide ($C_{12}H_{11}ClN_2O_5S$).

IDENTIFICATION

• **A.**

Standard stock solution: 0.4 mg/mL of USP Furosemide RS, prepared as follows. Transfer about 10 mg of USP Furosemide RS to a 25-mL volumetric flask. Add 6.0 mL of 0.1 N sodium hydroxide and dissolve. Dilute with water to volume.

Standard solution: 8 µg/mL of USP Furosemide RS from *Standard stock solution* in 0.02 N sodium hydroxide

Sample stock solution: Nominally 0.4 mg/mL of furosemide in water, prepared as follows. Transfer a volume of Injection, nominally equivalent to 40 mg of furosemide, to a 100-mL volumetric flask and dilute with water to volume.

Sample solution: Nominally 8 µg/mL of furosemide from *Sample stock solution* in 0.02 N sodium hydroxide

Analysis: Concomitantly determine the UV absorption spectra of *Standard solution* and *Sample solution*.

Acceptance criteria: The UV absorption spectra of *Standard solution* and *Sample solution* exhibit maxima and minima at the same wavelengths.

ASSAY

[Note—Protect furosemide solutions from exposure to light.]

• **Procedure**

Mobile phase: Tetrahydrofuran, glacial acetic acid, and water (30:1:70)

Solution A: Acetonitrile and water (50:50)

Diluent: Transfer 22 mL of glacial acetic acid to a suitable container and dilute with *Solution A* to 1000 mL.

System suitability solution: 20 µg/mL of USP Furosemide RS and 12 µg/mL of USP Furosemide Related Compound A RS in *Diluent*

Standard solution: 1.0 mg/mL of USP Furosemide RS in *Diluent*

Sample solution: Nominally 1.0 mg/mL of furosemide in *Diluent*, prepared as follows. Transfer a volume of Injection, nominally equivalent to 10 mg of furosemide, to a 10-mL volumetric flask and dilute with *Diluent* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm for furosemide and 272 nm

[Note—The 2,4-dichloro-5-sulfamoylbenzoic acid impurity does not respond at 272 nm and the 2,4-bis(furfurylamino)-5-sulfamoylbenzoic acid impurity has a very intense absorbance at 254 nm.]

Column: 4.6-mm × 25-cm; packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 2.5 between furosemide and furosemide related compound A

Relative standard deviation: NMT 2.0% for furosemide

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of furosemide ($C_{12}H_{11}ClN_2O_5S$) in the portion of Injection taken:

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

r_U = peak response of furosemide from the *Sample solution* at 254 nm

r_S = peak response of furosemide from the *Standard solution* at 254 nm

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

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

Acceptance criteria: 90.0%–110.0%

IMPURITIES

• **Limit of Furosemide Related Compound B**

[Note—Protect furosemide solutions from exposure to light.]

Mobile phase, Solution A, Diluent, System suitability solution, Sample solution, Chromatographic system and **System suitability:** Proceed as directed in the *Assay*.

Standard solution: 0.01 mg/mL of USP Furosemide Related Compound B RS in *Diluent*

Analysis

Samples: *Standard solution* and *Sample solution*

Compare the peak responses of furosemide related compound B obtained between the *Standard solution* and *Sample solution*.

Acceptance criteria: NMT 1.0% (the peak response at 254 nm of furosemide related compound B from the *Sample solution* is NMT that from the *Standard solution*)

Where the Injection is labeled as intended solely for veterinary use: NMT 2.5% (the peak response at 254 nm of furosemide related compound B from the *Sample solution* is NMT 2.5 times that from the *Standard solution*)

SPECIFIC TESTS

• **Bacterial Endotoxins Test ⟨85⟩:** It contains NMT 3.6 USP Endotoxin Units/mg of furosemide.

• **pH ⟨791⟩:** 8.0–9.3

Where the Injection is labeled as intended solely for veterinary use, and it contains diethanolamine: 7.0–7.8

Where the Injection is labeled as intended solely for veterinary use, and it contains monoethanolamine: 8.0–9.3

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

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

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Store in single-dose or multiple-dose, light-resistant containers, ▲preferably▲ (RB 1-Apr-2023) of Type I glass.

• **Labeling:** Injection intended solely for veterinary use is so labeled.

• **USP Reference Standards ⟨11⟩**

USP Furosemide RS

USP Furosemide Related Compound A RS

2-Chloro-4-*N*-furfurylamino-5-sulfamoylbenzoic acid.

$C_{12}H_{11}ClN_2O_5S$ 330.74

USP Furosemide Related Compound B RS

4-Chloro-5-sulfamoylanthranilic acid.

$C_7H_7ClN_2O_4S$ 250.66

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

Topic/Question	Contact	Expert Committee
FUROSEMIDE INJECTION	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. Information currently unavailable

Current DocID: GUID-4007C238-514A-47F6-B493-2363E7AFC1D8_5_en-US

DOI: https://doi.org/10.31003/USPNF_M34550_05_01

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