Furosemide Injection

Type of Posting	Notice of Intent to Revise
Posting Date	16-Dec-2022
Targeted Official Date	To Be Determined, Revision Bulletin
Expert Committee	Small Molecules 2

In accordance with the Rules and Procedures of the Council of Experts and the Pending Monograph Guideline, this is to provide notice that the Small Molecules 2 Expert Committee intends to revise the Furosemide Injection monograph.

Based on the supporting data received from a manufacturer awaiting FDA approval, the Expert Committee proposes to revise the upper pH limit from 9.3 to 9.6 in the *pH* test.

Additional editorial changes were made to update the monograph to current *USP* style.

The proposed revision is contingent on FDA approval of a product that meets the proposed monograph specifications. The proposed revision will be published as a Revision Bulletin and an official date will be assigned to coincide as closely as possible with the FDA approval of the associated product.

See below for additional information about the proposed text.[1]

Should you have any questions, please contact V. Durga Prasad, Associate Scientific Liaison (+91-40-4448-8723 or durgaprasad.v@usp.org).

[1] This text is not the official version of a *USP–NF* monograph and may not reflect the full and accurate contents of the currently official monograph. Please refer to the current edition of the *USP–NF* for official text.

USP provides this text to indicate changes that we anticipate will be made official once the product subject to this proposed revision under the Pending Monograph Program receives FDA approval. Once FDA approval is granted for the associated revision request, a Revision Bulletin will be posted that will include the changes indicated herein, as well as any changes indicated in the product's final approval, combined with the text of the monograph as effective on the date of approval. Any revisions made to a monograph under the Pending Monograph Program that are posted without prior publication for comment in the *Pharmacopeial Forum* must also meet the requirements outlined in the USP Guideline on Use of Accelerated Processes for Revisions to the *USP–NF*.

Notice of Intent to Revise
Official: To Be Determined

Furosemide Injection

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.

Change to read:

● **pH ⟨791⟩:** 8.0–▲9.6▲ (TBD)

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

- **Packaging and Storage:** Store in single-dose or multiple-dose, light-resistant containers, 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

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