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Bumetanide Injection

Change to read:

DEFINITION

Bumetanide Injection is a sterile solution of bumetanide in Water for Injection. ▲It may contain buffering agents, preservatives, and isotonicity agents.▲ (USP 1-May-2024) It contains NLT 90.0% and NMT 110.0% of the labeled amount of bumetanide ($C_{17}H_{20}N_2O_5S$).

IDENTIFICATION

Change to read:

• **A.** ▲The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2024)

Change to read:

• **B.** ▲The UV spectrum of the bumetanide peak of the *Sample solution* exhibits maxima and minima at the same wavelengths as those of the corresponding peak of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2024)

ASSAY

Change to read:

• **Procedure**

▲**Solution A:** 0.5% (v/v) formic acid in water prepared as follows. To a 1-L volumetric flask, add 5 mL of formic acid and dilute with water to volume.

Solution B: Methanol

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	60	40
2	60	40
10	20	80
15	20	80
15.1	60	40
20	60	40

Standard stock solution: 0.2 mg/mL of USP Bumetanide RS in methanol

Standard solution: 0.1 mg/mL of USP Bumetanide RS from the *Standard stock solution* in water

Sample solution: Nominally 0.1 mg/mL of bumetanide prepared as follows. Transfer a suitable amount of Injection to a suitable volumetric flask. Add methanol to about 40% of the total volume and dilute with water to volume.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 15-cm; 3.5-µm packing L1

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of bumetanide ($C_{17}H_{20}N_2O_5S$) in the portion of Injection taken:

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

r_U = peak response of bumetanide from the *Sample solution*

r_S = peak response of bumetanide from the *Standard solution*

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

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

▲ (USP 1-May-2024)

Acceptance criteria: 90.0%–110.0%

IMPURITIES

Change to read:

• **Organic Impurities**

▲**Solution A, Solution B,** and **Mobile phase:** Prepare as directed in the *Assay*.

Diluent: Methanol and water (40:60)

Standard stock solutions: 0.1 mg/mL each of USP Bumetanide RS, USP Bumetanide Related Compound A RS, and USP Bumetanide Related Compound B RS individually prepared as follows. Transfer suitable amounts each of USP Bumetanide RS, USP Bumetanide Related Compound A RS, and USP Bumetanide Related Compound B RS to separate suitable volumetric flasks. Add methanol to about 40% of the total volume of each flask to dissolve the solids. Dilute with water to volume.

System suitability solution: 0.25 µg/mL each of USP Bumetanide RS, USP Bumetanide Related Compound A RS, and USP Bumetanide Related Compound B RS from the corresponding *Standard stock solutions* in *Diluent*

Standard solution: 0.25 µg/mL each of USP Bumetanide RS and USP Bumetanide Related Compound A RS from the corresponding *Standard stock solutions* in *Diluent*

Sensitivity solution: 0.125 µg/mL each of USP Bumetanide RS and USP Bumetanide Related Compound A RS from the *Standard solution* in *Diluent*

Sample solution: Nominally 0.25 mg/mL of Bumetanide from Injection

Chromatographic system: Proceed as directed in the *Assay*, except for the *Injection volume*.

Injection volume: 50 µL

System suitability

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

Suitability requirements

[Note—The relative retention time for bumetanide related compound B with respect to bumetanide is 0.7.]

Resolution: NLT 20 between bumetanide related compound A and bumetanide related compound B, *System suitability solution*

Relative standard deviation: NMT 5.0% for each peak, *Standard solution*

Signal-to-noise ratio: NLT 10 for each peak, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of bumetanide related compound A in the portion of Injection taken:

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

r_U = peak response of bumetanide related compound A from the *Sample solution*

r_S = peak response of bumetanide related compound A from the *Standard solution*

C_S = concentration of USP Bumetanide Related Compound A RS in the *Standard solution* (mg/mL)

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

Calculate the percentage of any unspecified impurity in the portion of Injection taken:

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

r_U = peak response of any unspecified impurity from the *Sample solution*

r_S = peak response of bumetanide from the *Standard solution*

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

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

Acceptance criteria: See *Table 2*. The reporting threshold is 0.1%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Bumetanide related compound A	0.3	0.2
Bumetanide	1.0	—
Any unspecified impurity	—	0.2
Total impurities[a]	—	0.8

[a] Bumetanide related compound A is not included in the total impurities.

▲ (USP 1-May-2024)

SPECIFIC TESTS

Change to read:

• **Bacterial Endotoxins Test ⟨85⟩:** ▲Meets the requirements▲ (USP 1-May-2024)

• **pH ⟨791⟩:** 6.8–7.8

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

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in single-dose or multiple-dose containers, preferably of Type I glass, protected from light. ▲Store at controlled room temperature.▲ (USP 1-May-2024)

Change to read:

• **USP Reference Standards ⟨11⟩**

USP Bumetanide RS

USP Bumetanide Related Compound A RS

3-Amino-4-phenoxy-5-sulfamoylbenzoic acid.

$C_{13}H_{12}N_2O_5S$ 308.31

▲ USP Bumetanide Related Compound B RS

3-Nitro-4-phenoxy-5-sulfamoylbenzoic acid.

$C_{13}H_{10}N_2O_7S$ 338.29▲ (USP 1-May-2024)

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

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

Chromatographic Database Information: Chromatographic Database

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