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Bumetanide Tablets

DEFINITION
Bumetanide Tablets contain 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 ▲▲ (USP 1-May-2024) retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

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 stock solution: Nominally 0.2 mg/mL of bumetanide from Tablets (NLT 10) in a suitable amount of methanol. Initially mix well until the Tablets are disintegrated, centrifuge for about 10 min, and use the supernatant. Sonication may be necessary for complete disintegration.

Sample solution: Nominally 0.1 mg/mL of bumetanide from the *Sample stock solution* in water

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 Tablets 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%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Test 1

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Solution A: 7.505 g/L of glycine and 5.85 g/L of sodium chloride in water

Solution B: *Solution A*, 0.1 N hydrochloric acid, and water (4:1:45). Adjust, if necessary, with 0.1 N hydrochloric acid or 0.1 N sodium hydroxide to a pH of 2.9.

Standard solution: USP Bumetanide RS at a known concentration in *Medium*

Sample solution: Dilute with *Solution B* as needed.

Instrumental conditions

Mode: Fluorescence

Detectors

Excitation wavelength: 350 nm

Emission wavelength: 450 nm

Analysis

Samples: *Standard solution* and *Sample solution*

▲Calculate the percentage of the labeled amount of bumetanide ($C_{17}H_{20}N_2O_5S$) dissolved:

$$\text{Result} = (I_U/I_S) \times [C_S \times V \times (1/L)] \times 100$$

I_U = fluorescence intensity of the *Sample solution*

I_S = fluorescence intensity of the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

▲ (USP 1-May-2024)

Tolerances: NLT 85% (Q) of the labeled amount of bumetanide ($C_{17}H_{20}N_2O_5S$) is dissolved

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium, Apparatus 2, and **Time:** Proceed as directed in *Test 1*.

Buffer: 2.72 g/L of potassium phosphate, monobasic in water. Adjust with 1.8 N potassium hydroxide to a pH of 7.0.

Mobile phase: Acetonitrile and *Buffer* (30:70)

Diluent: Acetonitrile and water (50:50)

Standard stock solution: 55.5 µg/mL of USP Bumetanide RS in *Diluent*

Standard solution: (L/1000) µg/mL of USP Bumetanide RS in *Medium*, from *Standard stock solution*, where L is the label claim in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 222 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 35°

Flow rate: 1.5 mL/min

Injection volume: 100 µL

Run time: NLT 1.7 times the retention time of bumetanide

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of bumetanide ($C_{17}H_{20}N_2O_5S$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (1/L) \times 100$$

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)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (*Q*) of the labeled amount of bumetanide ($C_{17}H_{20}N_2O_5S$) is dissolved

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

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 250 µg/mL of bumetanide prepared as follows. To Tablets (NLT 10), in a suitable volumetric flask, add about 40% of the total volume of methanol. Shake well until the Tablets disintegrate, and dilute with water to volume. Centrifuge for NLT 10 min and use the supernatant.

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*

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

Suitability requirements

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 Tablets 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* (µg/mL)

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

Calculate the percentage of any unspecified impurity in the portion of Tablets 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* (µg/mL)

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

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in tight, light-resistant containers. ▲Store at controlled room temperature.▲ (USP 1-May-2024)

• **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.

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 TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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