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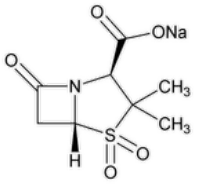
Sulbactam Sodium

Change to read:



$C_8H_{10}NNaO_5S$ 255.22

4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 3,3-dimethyl-7-oxo-, 4,4-dioxide, sodium salt, (2*S*-*cis*)-;

Sodium (2*S*,5*R*)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate 4,4-dioxide CAS RN®: 69388-84-7; UNII: DKQ4T82YE6.

▲Sulbactam (free acid)

$C_8H_{11}NO_5S$ 233.24 CAS RN®: 68373-14-8; UNII: S4TF6I2330.▲ (USP 1-Dec-2023)

DEFINITION

Sulbactam Sodium contains NLT 886 and NMT 941 µg/mg of sulbactam ($C_8H_{11}NO_5S$), calculated on the anhydrous basis.

IDENTIFICATION

Add the following:

▲• **A.** **Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K▲ (USP 1-Dec-2023)

Change to read:

• ▲**B.**▲ (USP 1-Dec-2023) The 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:

• ▲**C.**▲ (USP 1-Dec-2023) **Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Sodium*:** Meets the requirements

ASSAY

• **Procedure**

Buffer solution: 2.7 g/L of monobasic potassium phosphate, adjusted with dilute phosphoric acid to a pH of 4.0

Solution A: 5.4 g/L of monobasic potassium phosphate, adjusted with dilute phosphoric acid to a pH of 4.0

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	98	2
7.5	50	50
8.5	50	50
9.0	98	2

Time (min)	Solution A (%)	Solution B (%)
12.5	98	2

Standard solution: 0.7 mg/mL of USP Sulbactam RS prepared as follows. Dissolve a suitable amount of USP Sulbactam RS in acetonitrile, using 2% of the final volume, and dilute with *Buffer solution* to volume.

Sample solution: 0.77 mg/mL of Sulbactam Sodium prepared as follows. Dissolve a suitable amount of Sulbactam Sodium in acetonitrile, using 2% of the final volume, and dilute with *Buffer solution* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4-mm × 15-cm; 3-µm packing L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the quantity, in µg, of sulbactam ($C_8H_{11}NO_5S$) in each mg of Sulbactam Sodium taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

C_U = concentration of Sulbactam Sodium in the *Sample solution* (mg/mL)

P = potency of sulbactam in USP Sulbactam RS (mg/mg)

F = conversion factor, 1000 µg/mg

Acceptance criteria: 886–941 µg/mg on the anhydrous basis

IMPURITIES

Change to read:

• **Organic Impurities**

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

Diluent: 2 mL of acetonitrile diluted with *Buffer solution* to 100 mL

System suitability solution: 0.7 µg/mL each of USP Sulbactam Related Compound A RS, USP Sulbactam Related Compound D RS, USP Sulbactam Related Compound E RS, and USP Sulbactam Related Compound F RS, prepared as follows. Dissolve suitable amounts of USP Sulbactam Related Compound A RS, USP Sulbactam Related Compound D RS, USP Sulbactam Related Compound E RS, and USP Sulbactam Related Compound F RS in acetonitrile using 10% of the final volume, and sonicate as needed. Dilute with *Diluent* to volume. Protect this solution from light.

Standard stock solution: 0.7 mg/mL of USP Sulbactam RS prepared as follows. Dissolve a suitable amount of USP Sulbactam RS in acetonitrile, using 2% of the final volume, and dilute with *Buffer solution* to volume.

Standard solution: 0.7 µg/mL of USP Sulbactam RS from the *Standard stock solution*, in *Diluent*

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between sulbactam related compound D and sulbactam related compound E, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of each impurity in the portion of Sulbactam Sodium taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times P \times (1/F) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response from the *Standard solution*

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

C_U = concentration of Sulbactam Sodium in the *Sample solution* (mg/mL)

P = potency of sulbactam in USP Sulbactam RS (mg/mg)

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*. The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Sulbactam related compound A[a]	0.4	1.7	0.5
▲6-Aminopenicillanic acid▲ (USP 1-Dec-2023) (Amoxicillin related compound A)[b]	0.6	2.0	0.1
Sulbactam	1.0	—	—
6-Bromopenicillanic acid sulfone[c]	1.6	1.0	0.2
Sulbactam related compound D[d]	2.0	2.0	0.1
Sulbactam related compound E[e]	2.1	1.0	0.2
Sulbactam related compound F[f]	2.5	1.7	0.1
Any individual unspecified impurity	—	1.0	0.10
Total impurities	—	—	1.0

[a] 3-Sulfino-D-valine; (2*S*)-2-Amino-3-methyl-3-sulfinobutanoic acid.

[b] ▲▲ (USP 1-Dec-2023) (2*S*,5*R*,6*R*)-6-Amino-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid.

[c] (2*S*,5*R*,6*R*)-6-Bromo-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid 4,4-dioxide.

[d] 6-Bromopenicillanic acid; (2*S*,5*R*,6*R*)-6-Bromo-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid.

[e] 6,6-Dibromopenicillanic acid sulfone; also known as (2*S*,5*R*)-6,6-Dibromo-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid 4,4-dioxide.

[f] 6,6-Dibromopenicillanic acid; also known as (2*S*,5*R*)-6,6-Dibromo-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid.

SPECIFIC TESTS

• **Crystallinity ⟨695⟩:** Meets the requirements

Change to read:

• **Bacterial Endotoxins Test ⟨85⟩:** Where the label states that Sulbactam Sodium is sterile or must be subjected to further processing during the preparation of injectable dosage forms, ▲the level of bacterial endotoxins is such that the requirement under the relevant dosage form monograph(s) in which Sulbactam Sodium is used can be met.▲ (USP 1-Dec-2023)

Change to read:

• **Sterility Tests ⟨71⟩:** Where the label states that Sulbactam Sodium is sterile, it meets the requirements. ▲▲ (USP 1-Dec-2023)

• **Water Determination ⟨921⟩, *Method I*:** NMT 1.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.

• **Labeling:** Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms.

Change to read:

• **USP Reference Standards ⟨11⟩**

USP Sulbactam RS

▲USP Sulbactam Sodium RS▲ (USP 1-Dec-2023)

USP Sulbactam Related Compound A RS

(2*S*)-2-Amino-3-methyl-3-sulfinobutanoic acid.

$C_5H_{11}NO_4S$ 181.21

USP Sulbactam Related Compound D RS

(2*S*,5*R*,6*R*)-6-Bromo-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, potassium salt.

$C_8H_9BrKNO_3S$ 318.23

USP Sulbactam Related Compound E RS

(2*S*,5*R*)-6,6-Dibromo-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid 4,4-dioxide.

$C_8H_9Br_2NO_5S$ 391.03

USP Sulbactam Related Compound F RS

(2*S*,5*R*)-6,6-Dibromo-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid.

$C_8H_9Br_2NO_3S$ 359.03

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

Topic/Question	Contact	Expert Committee
SULBACTAM SODIUM	Documentary Standards Support	SM12020 Small Molecules 1
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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