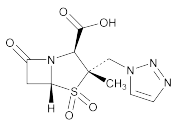
Tazobactam

Change to read:



$C_{10}H_{12}N_4O_5S$ 300.29
4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 3-methyl-7-oxo-3-(1*H*-1,2,3-triazol-1-ylmethyl)-, 4,4-dioxide, [2*S*-(2α,3*β*,5α)]-;
(2*S*,3*S*,5*R*)-3-Methyl-7-oxo-3-(1*H*-1,2,3-triazol-1-ylmethyl)-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 4,4-dioxide [89786-04-9].

•$C_{10}H_{12}N_4O_5S \cdot {}^1/_2H_2O$ 309.30
[428863-55-2].• (RB 1-May-2011)

DEFINITION

Tazobactam contains NLT 98.0% and NMT 102.0% of $C_{10}H_{12}N_4O_5S$, calculated on the anhydrous basis.

IDENTIFICATION

- **A. Infrared Absorption** ⟨197K⟩
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

Mobile phase: Dissolve 1.32 g of dibasic ammonium phosphate in 750 mL of water. Adjust with 5% v/v phosphoric acid to a pH of 2.5, and dilute with water to 1000 mL. Add 30 mL of acetonitrile, mix, and pass through a filter of 0.2-µm pore size.

System suitability solution: 16 µg/mL of L-phenylalanine, 50 µg/mL of USP Tazobactam RS, and 8 µg/mL of USP Tazobactam Related Compound A RS in *Mobile phase*. Maintain the *System suitability solution* at 3° until injection. Prepare fresh daily. If an autosampler is used, replace the plastic tubing connected to the injection needle with a stainless steel assembly, and maintain at 3°. If a chilled autosampler is not used, then this solution should be injected immediately after preparation.

Standard solution: 0.5 mg/mL of USP Tazobactam RS in *Mobile phase*. Cool and maintain the *Standard solution* at 3° until injection. If an autosampler is used, replace the plastic tubing connected to the injection needle with a stainless steel assembly, and maintain at 3°. If a chilled autosampler is not used, then this solution should be injected immediately after preparation.

Sample solution: 0.5 mg/mL of Tazobactam in *Mobile phase*. Cool and maintain the *Sample solution* at 3° until injection. If an autosampler is used, replace the plastic tubing connected to the injection needle with a stainless steel assembly, and maintain at 3°. If a chilled autosampler is not used, then this solution should be injected immediately after preparation.

Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 210 nm
Column: 4.6-mm × 25-cm; 5-µm packing L1
Flow rate: 1.5 mL/min
Injection size: 20 µL
System suitability
Samples: *System suitability solution* and *Standard solution*
[Note—See *Table 1* for the relative retention times.]
Suitability requirements
Resolution: NLT 6.0 between tazobactam and L-phenylalanine, *System suitability solution*
Tailing factor: NMT 1.8, *Standard solution*
Relative standard deviation: NMT 2.0%, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of tazobactam ($C_{10}H_{12}N_4O_5S$) in the portion of Tazobactam taken:

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

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Tazobactam RS in the *Standard solution* (mg/mL)
C_U = concentration of the *Sample solution* (mg/mL)
Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

- **Residue on Ignition** ⟨281⟩**:** NMT 0.1%
- **Heavy Metals,** *Method II* ⟨231⟩**:** NMT 20 ppm
- **Organic Impurities**

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

Blank: *Mobile phase*. Cool and maintain the *Blank* at 3° until injection. If an autosampler is used, replace the plastic tubing connected to the injection needle with a stainless steel assembly, and maintain at 3°. If a chilled autosampler is not used, then this solution should be injected immediately after preparation.

Sample solution: Prepare as directed in the *Assay*. Cool and maintain the *Sample solution* at 3° until injection. If an autosampler is used, replace the plastic tubing connected to the injection needle with a stainless steel assembly, and maintain at 3°. If a chilled autosampler is not used, then this solution should be injected immediately after preparation.

Analysis
Samples: *Blank* and *Sample solution*
Ignore any peaks of the *Sample solution* that correspond to any peaks of the *Blank*.
Calculate the percentage of each impurity in the portion of Tazobactam taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response for each impurity in the *Sample solution*
r_T = sum of all the peak responses in the *Sample solution*

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Tazobactam related compound A	0.29	1.0
L-Phenylalanine	0.71	—
Tazobactam	1.0	—
Any other individual impurity	—	0.1
Total impurities[a]	—	0.3

[a] Total of all impurities other than tazobactam related compound A.

SPECIFIC TESTS

- **BACTERIAL ENDOTOXINS TEST ⟨85⟩:** The level of bacterial endotoxins is such that the requirements of the relevant dosage form monograph(s) in which Tazobactam is used can be met.
- **OPTICAL ROTATION,** *Specific Rotation* ⟨**781S**⟩
  Sample solution: 10 mg/mL, in dimethylformamide
  Acceptance criteria: +160° to +167° (t = 20°)
- **MICROBIAL ENUMERATION TESTS ⟨61⟩** and **TESTS FOR SPECIFIED MICROORGANISMS ⟨62⟩:** The total aerobic microbial count does not exceed 10^3 cfu/g, and the total combined molds and yeasts count does not exceed 10^2 cfu/g.
- **pH ⟨791⟩**
  Sample solution: 2.5 mg/mL
  Acceptance criteria: 1.8–2.8

Change to read:

- **WATER DETERMINATION,** *Method I* ⟨**921**⟩**:** NMT 0.6% •for the anhydrous form; 2.2–3.8% for the hemihydrate form•(RB 1-May-2011)

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers. Store at controlled room temperature.

Add the following:

•• **LABELING:** Where it is the hemihydrate form, the label so indicates.• (RB 1-May-2011)

- **USP REFERENCE STANDARDS ⟨11⟩**
  USP Endotoxin RS
  USP Tazobactam RS
  USP Tazobactam Related Compound A RS
  (2*S*,3*S*)-2-Amino-3-methyl-3-sulfino-4-(1*H*-1,2,3-triazol-1-yl)butyric acid.
  $C_7H_{12}N_4O_4S$ 248.26