F = conversion factor, 0.001 mg/µg

Where packaged in a multiple-unit container

Calculate the percentage of the labeled amount of azithromycin ($C_{38}H_{72}N_2O_{12}$) in the portion of Azithromycin for Oral Suspension taken:

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

r_U = peak response from *Sample solution 2*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Azithromycin RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of azithromycin in *Sample solution 2* (mg/mL)
P = potency of azithromycin in USP Azithromycin RS (µg/mg)
F = conversion factor, 0.001 mg/µg

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

- **DELIVERABLE VOLUME** ⟨**698**⟩**:** Meets the requirements
- **UNIFORMITY OF DOSAGE UNITS** ⟨**905**⟩**:** Meets the requirements for a solid packaged in single-unit containers

SPECIFIC TESTS

- **pH** ⟨**791**⟩
  For a solid packaged in single-unit containers: 9.0–11.0, in the suspension constituted as directed in the labeling
  For a solid packaged in multiple-unit containers: 8.5–11.0, in the suspension constituted as directed in the labeling
- **WATER DETERMINATION,** *Method I* ⟨**921**⟩**:** NMT 1.5%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Azithromycin RS
  USP Azaerythromycin RS

Azithromycin Tablets

DEFINITION

Azithromycin Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of azithromycin ($C_{38}H_{72}N_2O_{12}$).

IDENTIFICATION

- 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**
  Solution A: A solution containing 4.4 mg/mL of dibasic potassium phosphate and 0.5 mg/mL of sodium 1-octanesulfonate. Adjust with phosphoric acid to a pH of 8.20 ± 0.05.
  Mobile phase: Acetonitrile, methanol, and *Solution A* (9:3:8)
  Solution B: 1.7 mg/mL of monobasic ammonium phosphate. Adjust with ammonium hydroxide to a pH of 10.00 ± 0.05.
  Diluent A: Methanol, acetonitrile, and *Solution B* (7:6:7)
  Standard solution: Dissolve USP Azithromycin RS in *Diluent A* using about 75% of the final volume, sonicate to dissolve, dilute with *Diluent A* to volume, and mix to obtain a solution having a known concentration of 0.4 mg/mL of azithromycin.
  System suitability stock solution: 0.2 mg/mL of USP Azaerythromycin A RS in acetonitrile. [NOTE—Sonicate if necessary to dissolve.]
  System suitability solution: 0.02 mg/mL of azaerythromycin A from the *System suitability stock solution* and 0.02 mg/mL of azithromycin from the *Standard solution* in *Diluent A*
  Sample stock solution: Weigh and finely powder NLT 20 Tablets. Transfer an equivalent to 667 mg of azithromycin to a 200-mL volumetric flask. Add 75 mL of *Diluent A*, and sonicate for NLT 15 min. Shake by mechanical means for NLT 15 min. Allow the solution to equilibrate to room temperature, dilute with *Diluent A* to volume, and mix.
  Sample solution: 0.4 mg/mL of azithromycin from the *Sample stock solution* in *Diluent A*. Pass through a filter of 0.45-µm pore size.
  Chromatographic system
  (See *Chromatography* ⟨621⟩*, System Suitability*.)
  Mode: LC
  Detector: UV 210 nm
  Column: 4.6-mm × 25-cm; 5-µm packing L1
  Column temperature: 50°
  Flow rate: 1.5 mL/min
  Injection size: 50 µL
  System suitability
  Samples: *Standard solution* and *System suitability solution*
  [NOTE—Identify the peaks by their relative retention times, which are 0.64 and 1.0 for azaerythromycin A and azithromycin, respectively.]
  Suitability requirements
  Resolution: NLT 2.5 between azaerythromycin A and azithromycin, *System suitability solution*
  Column efficiency: NLT 1000 theoretical plates, *Standard solution*
  Tailing factor: NMT 2.0, *Standard solution*
  Relative standard deviation: NMT 2.0%, *Standard solution*
  Analysis
  Samples: *Standard solution* and *Sample solution*
  Calculate the percentage of $C_{38}H_{72}N_2O_{12}$ in the portion of Tablets taken:

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

r_U = peak response of azithromycin from the *Sample solution*
r_S = peak response of azithromycin from the *Standard solution*
C_S = concentration of USP Azithromycin RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of azithromycin in the *Sample solution* (mg/mL)
P = potency of USP Azithromycin RS (µg/mg)
F = unit conversion factor, 0.001 mg/µg

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

- **DISSOLUTION** ⟨**711**⟩
  Medium: pH 6.0 phosphate buffer; 900 mL
  Apparatus 2: 75 rpm
  Time: 30 min
  Solution A and **Mobile phase:** Proceed as directed in the *Assay*.
  Diluent: 17.5 mg/mL of dibasic potassium phosphate. Adjust with phosphoric acid to a pH of 8.00 ± 0.05. Prepare a mixture of this solution and acetonitrile (80:20).
  Standard stock solution: Dissolve USP Azithromycin RS in *Medium* to obtain a solution having a known concentration of about (L/1000) mg/mL, where L is the Tablet label claim, in mg.
  Standard solution: Dilute the *Standard stock solution* with *Diluent* to obtain a solution having a known concentration of about (L/2000) mg/mL, where L is the Tablet label claim, in mg.
  Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Dilute a portion of the filtrate with *Diluent* to obtain a

solution having a theoretical concentration of about (L/2000) mg/mL, where L is the Tablet label claim, in mg, assuming complete dissolution.

Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 210 nm
Column: 4.6-mm × 15-cm; 5-µm packing L1
Column temperature: 50°
Flow rate: 1.5 mL/min
Injection size: 50 µL
System suitability
Sample: *Standard solution*
Suitability requirements:
Column efficiency: NLT 1000 theoretical plates
Tailing factor: NMT 2.0
Relative standard deviation: NMT 2.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Determine the amount of $C_{38}H_{72}N_2O_{12}$ dissolved:

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

r_U = peak response of azithromycin from the *Sample solution*
r_S = peak response of azithromycin from the *Standard solution*
C_S = concentration of the *Standard solution* (mg/mL)
L = Tablet label claim (mg)
V = volume of *Medium*, 900 mL

Tolerances: NLT 80% (Q) of the labeled amount of $C_{38}H_{72}N_2O_{12}$ is dissolved.

• **UNIFORMITY OF DOSAGE UNITS** ⟨**905**⟩**:** Meet the requirements

IMPURITIES

Organic Impurities

• **PROCEDURE**
[NOTE— Use low-actinic glassware. Refrigerate the *Standard solution* and the *Sample solution* after preparation and during analysis, using a refrigerated autosampler set at 4°. The solutions must be analyzed within 24 h of preparation.]
Solution B, **Diluent A**, and **System suitability solution:** Proceed as directed in the *Assay*.
Solution C: 1.8 mg/mL of dibasic sodium phosphate in water
Solution D: Acetonitrile and methanol (3:1)
Mobile phase: See the gradient table below.

Time (min)	Solution C (%)	Solution D (%)
0	50	50
25	50	50
30	45	55
40	40	60
55	35	65
60	35	65
61	50	50
70	50	50

Diluent B: Methanol and *Solution B* (1:1)
Blank: Use *Diluent A*.
Standard stock solution: Use the *Standard solution* as directed in the *Assay*.
Standard solution: 0.02 mg/mL of azithromycin from the *Standard stock solution* in *Diluent A*
Sensitivity solution: 0.004 mg/mL of azithromycin from the *Standard solution* in *Diluent A*
Sample stock solution: Weigh and finely powder NLT 20 Tablets. Transfer an equivalent to 1335 mg of azithromycin to a 100-mL volumetric flask. Add 75 mL of acetonitrile, and sonicate for NLT 15 min. Shake by mechanical means for NLT 15 min. Allow the solution to equilibrate to room temperature, dilute with acetonitrile to volume, and mix.
Sample solution: Centrifuge an aliquot of the *Sample stock solution* for 15 min. Transfer 3.0 mL of the supernatant to a 10-mL volumetric flask, dilute with *Diluent B* to volume, and mix to obtain a solution having a nominal concentration of about 4 mg/mL of azithromycin. Pass through a filter of 0.45-µm pore size.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 210 nm
Column: 4.6-mm × 25-cm; 5-µm packing L1
Column temperature: 60°
Flow rate: 0.8 mL/min
Autosampler temperature: 4°
Injection size: 100 µL
System suitability
Samples: *System suitability solution*, *Standard solution*, and *Sensitivity solution*
Suitability requirements
Signal-to-noise ratio: NLT 10, *Sensitivity solution*
Resolution: NLT 2.5 between azaerythromycin A and azithromycin, *System suitability solution*
Relative standard deviation: NMT 10.0%, *Standard solution*
Analysis
Samples: *Blank* and *Sample solution*
Calculate the percentage of each impurity in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times P \times F_1 \times (1/F_2) \times 100$$

r_U = peak response of each impurity from the *Sample solution*
r_S = peak response of azithromycin from the *Standard solution*
C_S = concentration of USP Azithromycin RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of azithromycin in the *Sample solution* (mg/mL)
P = potency of USP Azithromycin RS (µg/mg)
F_1 = unit conversion factor, 0.001 mg/µg
F_2 = relative response factor (see *Impurity Table 1*)

Acceptance criteria
[NOTE—The reporting level for impurities is 0.1%. Disregard any peaks in the *Sample solution* that correspond to peaks in the *Blank*.]
Individual impurities: See *Impurity Table 1*.
Total impurities: See *Impurity Table 1*.

Impurity Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Azithromycin 3′-*N*-oxide	0.28	0.45	1.0
3′-(*N,N*-Didemethyl)-3′-*N*-formylazithromycin	0.38	1.9	1.0
3′-(*N,N*-Didemethyl) azithromycin (aminoazithromycin)	0.40	0.52	0.5
Desosaminylazithromycin	0.47	1.1	0.5

[a] 3′-(*N*-Demethyl)-3′-*N*-formylazithromycin.
[b] These compounds are synthetic process impurities of azithromycin. They are controlled in the drug substance and are listed here for information only. The total impurities specification does not include these impurities.

Impurity Table 1 *(Continued)*

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Azithromycin related compound F[a]	0.53	4.8	1.0
3′-*N*-Demethyl-azithromycin	0.57	0.53	0.7
3′-De(dimethyl-amino)-3′-oxo-azithromycin	0.78	1.6	1.0
6-Demethylazithro-mycin (azaerythro-mycin A)[b]	0.82	—	—
Azithromycin	1.0	—	—
3-Deoxyazithro-mycin (azithro-mycin B)[b]	1.3	—	—
3′-*N*-Demethyl-3′-*N*-[(4-methylphenyl)-sulfonyl] azithromycin[b]	1.4	—	—
Any other unspeci-fied impurity	—	1.0	0.2
Total impurities[b]	—	—	5.0

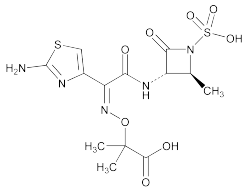
[a] 3′-(*N*-Demethyl)-3′-*N*-formylazithromycin.

[b] These compounds are synthetic process impurities of azithromycin. They are controlled in the drug substance and are listed here for information only. The total impurities specification does not include these impurities.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers. Store at controlled room temperature.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Azaerythromycin A RS
  USP Azithromycin RS

Aztreonam



$C_{13}H_{17}N_5O_8S_2$ 435.43

Propanoic acid, 2-[[[1-(2-amino-4-thiazolyl)-2-[(2-methyl-4-oxo-1-sulfo-3-azetidinyl)amino]-2-oxoethylidene]amino]oxy]-2-methyl-, [2*S*-[2α,3β(*Z*)]]-;
(*Z*)-2-[[[(2-Amino-4-thiazolyl)[[(2*S*,3*S*)-2-methyl-4-oxo-1-sulfo-3-azetidinyl]carbamoyl]methylene]amino]oxy]-2-methylpropionic acid [78110-38-0].

DEFINITION

Aztreonam, which may be anhydrous or hydrated, contains NLT 92.0% and NMT 105.0% of $C_{13}H_{17}N_5O_8S_2$, calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

- **INFRARED ABSORPTION** ⟨**197K**⟩**:** If a difference appears in the IR spectra of the analyte and the standard, dissolve equal portions of the test specimen and the reference standard in equal volumes of methanol. [NOTE—To achieve a complete dissolution, it is suggested to use about 25 mL of methanol for each 50 mg of material, and stir the mixture for 40 min at room temperature.] Evaporate the solutions to dryness under vacuum, and dry at 40° for 4 h under vacuum. Perform the test on the residues.

ASSAY

- **PROCEDURE**

[NOTE—Store the *System suitability solution*, *Standard solution*, and *Sample solution* at 5°, and protect from light to prevent isomerization of aztreonam *Z*-isomer to aztreonam *E*-isomer.]

Buffer: 6.8 mg/mL of monobasic potassium phosphate in water. Adjust with 1 M phosphoric acid to a pH of 3.0.

Mobile phase: Methanol and *Buffer* (1:4)

System suitability solution: 1 mg/mL of USP Aztreonam RS and 1 mg/mL of USP Aztreonam *E*-Isomer RS in *Mobile phase*

Standard solution: 1 mg/mL of USP Aztreonam RS in *Mobile phase*

Sample solution: 1 mg/mL of Aztreonam in *Mobile phase*

Chromatographic system
(See *Chromatography* ⟨621⟩*, System Suitability*.)
Mode: LC
Detector: UV 254 nm
Column: 3.9-mm × 30-cm; 10-µm packing L1
Flow rate: 1.5 mL/min
Injection size: 10 µL

System suitability
Samples: *System suitability solution* and *Standard solution*
[NOTE—The relative retention times for aztreonam and aztreonam *E*-isomer are 1.0 and 1.8, respectively.]
Suitability requirements
Resolution: NLT 2.0 between aztreonam and aztreonam *E*-isomer, *System suitability solution*
Tailing factor: NMT 2 for aztreonam, *System suitability solution*
Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of aztreonam ($C_{13}H_{17}N_5O_8S_2$) in the portion of Aztreonam taken:

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

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Aztreonam RS in the *Standard solution* (mg/mL)
C_U = concentration of Aztreonam in the *Sample solution* (mg/mL)
P = potency of USP Aztreonam RS (µg/mg)
F = unit conversion factor, 0.001 mg/µg

Acceptance criteria: 92.0%–105.0% on the anhydrous and solvent-free basis

IMPURITIES

Inorganic Impurities

- **RESIDUE ON IGNITION** ⟨**281**⟩**:** NMT 0.1%, the charred residue being moistened with 2 mL of nitric acid and 5 drops of sulfuric acid
- **HEAVY METALS,** *Method II* ⟨**231**⟩**:** NMT 30 ppm

Organic Impurities

- **PROCEDURE**

[NOTE— Store the *System suitability solution*, *Standard solution*, and *Sample solution* at 5°, and protect from light to