Status: Currently Official on 13-Feb-2025
Official Date: Official Prior to 2013
Document Type: USP Monographs
DocId: GUID-1A9EFB97-EB37-4775-BD15-7639619B1735_1_en-US
DOI: https://doi.org/10.31003/USPNF_M6745_01_01
DOI Ref: ux174

Azithromycin Capsules

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

IDENTIFICATION
• **A.** The retention time of the azithromycin peak of the *Sample solution* corresponds to that of the *Standard solution,* as obtained in the *Assay.*

ASSAY
• **Procedure**
[Note—Use water that has a resistivity of NLT 18 Mohm-cm.]

Mobile phase: Dissolve 5.8 g of monobasic potassium phosphate in 2130 mL of water, and add 870 mL of acetonitrile. Adjust with about 6 mL of 10 N potassium hydroxide to a pH of 11.0 ± 0.1, and pass through a suitable filter.

Standard stock solution: 0.165 mg/mL of USP Azithromycin RS in acetonitrile. Swirl, and sonicate as necessary.

Standard solution: 3.3 µg/mL of USP Azithromycin RS from the *Standard stock solution* in *Mobile phase*

System suitability stock solution: 0.16 mg/mL of USP Azaerythromycin A RS in acetonitrile and *Mobile phase* (1:9). Dissolve first in acetonitrile, using 10% of the final volume. Swirl, and sonicate to dissolve. Dilute with *Mobile phase* to volume.

System suitability solution: 3.2 µg/mL of azaerythromycin A from the *System suitability stock solution* and 3.3 µg/mL of azithromycin from the *Standard stock solution* in *Mobile phase*

Sample stock solution: Remove, as completely as possible, the contents of NLT 20 Capsules. Prepare a 1-mg/mL solution of anhydrous azithromycin in acetonitrile. Dissolve a portion of the mixed Capsule contents first in 70% of the final volume of acetonitrile, and shake by mechanical means for 30 min. Dilute with acetonitrile to volume. Place 40 mL of the resulting suspension in a centrifuge tube, and centrifuge. Use the supernatant to prepare the *Sample solution*.

Sample solution: 3.2 µg/mL of azithromycin from the *Sample stock solution* in *Mobile phase*

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

Mode: LC

Detector: Amperometric electrochemical detector

Electrode: Dual glassy carbon electrodes

Mode: Oxidative screen mode

Electrode 1: +0.70 ± 0.05 V

Electrode 2: +0.82 ± 0.05 V

Background current: 85 ± 15 nanoampheres

Columns

Guard: 4.6-mm × 5-cm; 5-µm packing L29

Analytical: 4.6-mm × 15-cm; 5-µm packing L29 or 3-µm packing L49 without the guard column

Flow rate: 1.5 mL/min

Injection size: 50 µL

System suitability

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

[Note—The relative retention times for azaerythromycin A and azithromycin with the L29 column are 0.7 and 1.0, respectively; the relative retention times for azaerythromycin A and azithromycin with the L49 column are 0.8 and 1.0, 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: 0.9–1.5, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of azithromycin ($C_{38}H_{72}N_2O_{12}$) in the portion of Capsules 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 Azithromycin RS in the *Standard solution* (µg/mL)

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

• **Dissolution** ⟨711⟩

[Note—Use water that has a resistivity of NLT 18 Mohm-cm.]

Medium: pH 6.0 sodium phosphate buffer (Prepare 6 L of 0.1 M dibasic sodium phosphate. Adjust with about 40 mL of hydrochloric acid to a pH of 6.0 ± 0.05, and add 600 mg of trypsin); 900 mL

Apparatus 2: 100 rpm

Time: 45 min

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

Standard stock solution: 0.3 mg/mL of USP Azithromycin RS in *Medium*. Sonicate briefly to dissolve.

Standard solution: 3.84 µg/mL of azithromycin from the *Standard stock solution* in *Mobile phase*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.5-µm or finer pore size. Transfer 2.0 mL of the filtrate to a 25-mL volumetric flask, and dilute with *Mobile phase* to volume. Transfer 4.0 mL of this solution to a second 25-mL volumetric flask, and dilute with *Mobile phase* to volume.

Analysis

Samples: *Standard solution* and *Sample solution*

Determine the amount of azithromycin ($C_{38}H_{72}N_2O_{12}$) dissolved using the procedure in the *Assay,* making any necessary modifications.

Calculate the percentage of azithromycin ($C_{38}H_{72}N_2O_{12}$) dissolved:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

L = label claim (mg/Capsule)

D = dilution factor of the *Sample solution*

V = volume of *Medium*, 900 mL

Tolerances: NLT 75% (*Q*) of the labeled amount of azithromycin ($C_{38}H_{72}N_2O_{12}$) is dissolved.

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

SPECIFIC TESTS

• **Water Determination,** *Method I*⟨921⟩**:** NMT 5.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Where packaged in unit-of-use containers, each container contains six 250-mg Capsules, and the label indicates the intended sequential day of use for each Capsule.

• **USP Reference Standards** ⟨11⟩

USP Azaerythromycin A RS

USP Azithromycin RS

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

Topic/Question	Contact	Expert Committee
AZITHROMYCIN CAPSULES	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 27(6)

Current DocID: GUID-1A9EFB97-EB37-4775-BD15-7639619B1735_1_en-US
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