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Azithromycin for Oral Suspension

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<https://www.uspnf.com/rb-azithromycin-for-os-20240426>.

DEFINITION

Azithromycin for Oral Suspension is a dry mixture of Azithromycin and one or more buffers, sweeteners, diluents, anticaking agents, and flavors. It contains 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.
- **B. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197A

Standard: 25 mg/mL of [USP Azithromycin RS](#) in [acetonitrile](#). Pass the solution through a suitable filter, and remove the solvent by natural evaporation.

Sample: Equivalent to 25 mg/mL of azithromycin from Azithromycin for Oral Suspension in [acetonitrile](#). Pass the solution through a suitable filter, and remove the solvent by natural evaporation.

Analysis: Examine the spectra of the *Standard* and the *Sample* in the range between 3800 and 650 cm^{-1} .

Acceptance criteria: The *Sample* exhibits bands at about 900, 995, 1165, 1376, 1456, 1725, and 2936 cm^{-1} similar to the spectrum from the *Standard* similarly obtained.

ASSAY

PROCEDURE

[NOTE—Solutions containing azithromycin are stable up to 12 h at 10°.]

Solution A: Dissolve 8.7 g of [dipotassium hydrogen phosphate anhydrous](#) in 1000 mL of [water](#) and adjust with [potassium hydroxide](#) or dilute [phosphoric acid](#) to a pH of 8.2.

Solution B: [Acetonitrile](#)

Mobile phase: *Solution A* and *Solution B* (30:70)

Diluent: [Acetonitrile](#), [methanol](#), and [water](#) (40:40:20)

Standard solution: 0.6 mg/mL of [USP Azithromycin RS](#) in *Diluent*. Sonicate in cool water to dissolve as needed.

Sample solution: Nominally 0.6 mg/mL of azithromycin in *Diluent* prepared as follows. Transfer an accurately measured portion of the constituted suspension to a suitable volumetric flask. Add *Diluent* equal to 50% of the volume of the flask, and sonicate for 20 min with shaking in cool water. Dilute with *Diluent* to volume. Pass a portion of this solution through a suitable filter of 0.45- μm pore size.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm $\times$ 25-cm; 5- μm packing [L1](#)

Temperatures

Autosampler: 10°

Column: 30°

Flow rate: 2 mL/min

Injection volume: 50 μL

Run time: NLT 2 times the retention time of azithromycin

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 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 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 = 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):**

For single-unit containers: Meets the requirements

Change to read:

- **DISSOLUTION (711):**

▲Test 1▲ (RB 1-May-2024)

[NOTE—Solutions containing azithromycin are stable up to 12 h at 10°.]

Medium: Sodium phosphate buffer, pH 6.0 (14.2 g/L of [sodium phosphate, dibasic, anhydrous](#) in [water](#), adjusted with [dilute hydrochloric acid](#) to pH 6.0); 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Solution A: Dissolve 8.7 g of [dipotassium hydrogen phosphate anhydrous](#) in 1000 mL of [water](#) and adjust with [potassium hydroxide](#) or dilute [phosphoric acid](#) to a pH of 8.2.

Solution B: [Acetonitrile](#)

Mobile phase: *Solution A* and *Solution B* (35:65)

Standard stock solution: 0.55 mg/mL of [USP Azithromycin RS](#) prepared as follows. Transfer an accurately weighed amount of [USP Azithromycin RS](#) to a suitable volumetric flask. Add [acetonitrile](#) to fill 5% of the volume of the flask and sonicate in cool water for 5 min to dissolve completely. Dilute with *Medium* to volume.

Standard solution

For Azithromycin for Oral Suspension labeled to contain 100 mg/5 mL: 0.11 mg/mL of [USP Azithromycin RS](#) in *Medium* from *Standard stock solution*

For Azithromycin for Oral Suspension labeled to contain 200 mg/5 mL: 0.22 mg/mL of [USP Azithromycin RS](#) in *Medium* from *Standard stock solution*

Sample solution: Pass a portion of the solution under test through a suitable filter.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 15-cm; 5-µm packing [L1](#)

Temperatures

Autosampler: 10°

Column: 50°

Flow rate: 2 mL/min

Injection volume: 100 µL

Run time: NLT 2 times the retention time of azithromycin

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 (Q) of the labeled amount of azithromycin ($C_{38}H_{72}N_2O_{12}$) dissolved:

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

r_U = peak response of azithromycin from the *Sample solution*

r_s = peak response of azithromycin from the *Standard solution*

C_s = concentration of [USP Azithromycin RS](#) in the *Standard solution* (mg/mL)

L = label claim of Azithromycin for Oral Suspension (mg/5 mL)

D = dilution factor, necessary only if the *Sample solution* requires dilution (mL/mL)

d = density of the *Sample solution* (g/mL)

W = weight of Azithromycin for Oral Suspension taken (g)

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.

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

[NOTE—Solutions containing azithromycin may be stable for 72 h at 10°.]

Medium: Sodium phosphate buffer, pH 6.0 (14.2 g/L of [sodium phosphate, dibasic, anhydrous](#) in [water](#), adjusted with [dilute hydrochloric acid](#) to a pH of 6.0); 900 mL

Apparatus 2: 25 rpm

Time: 45 min

Buffer: Dissolve 8.7 g of [dipotassium hydrogen phosphate anhydrous](#) in 1000 mL of [water](#). Adjust with [potassium hydroxide](#) or dilute [phosphoric acid](#) to a pH of 8.2.

Mobile phase: [Acetonitrile](#) and *Buffer* (65:35)

Standard stock solution: 0.55 mg/mL of [USP Azithromycin RS](#) prepared as follows. Transfer a quantity of [USP Azithromycin RS](#) to an appropriate volumetric flask and dissolve in 5% of the flask volume of [acetonitrile](#). Sonicate in cool water for about 5 min. Dilute with *Medium* to volume.

Standard solution

For Azithromycin for Oral Suspension constituted to 100 mg/5 mL: 0.11 mg/mL of [USP Azithromycin RS](#) from *Standard stock solution* in *Medium*

For Azithromycin for Oral Suspension constituted to 200 mg/5 mL: 0.22 mg/mL of [USP Azithromycin RS](#) from *Standard stock solution* in *Medium*

Sample solution: Proceed constitution as directed in the *Labeling*. Determine the density, d (g/mL), of the constituted suspension using appropriate means. Using a suitable syringe, collect approximately 5 mL of suspension, and record the weight. With the paddles lowered, gently add the collected suspension into each vessel containing the *Medium*. Start rotating the paddles. Reweigh the syringe, and determine the weight, W (g), of suspension delivered into each vessel. At the end of 45 min, withdraw a suitable volume of the solution under test. Pass through a suitable filter, discarding an appropriate volume of filtrate so that a consistent result can be obtained.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 15-cm; 5-μm packing [L1](#)

Temperatures

Autosampler: 10°

Column: 50°

Flow rate: 2 mL/min

Injection volume: 100 μL

Run time: NLT 2 times the retention time of azithromycin

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 azithromycin ($C_{38}H_{72}N_2O_{12}$) dissolved:

$$\text{Result} = (r_u/r_s) \times C_s \times V \times (d/W) \times (1/L) \times 100$$

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)