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Azithromycin for Injection

DEFINITION

Azithromycin for Injection is a sterile, dry mixture of azithromycin and a suitable stabilizing agent. 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 major 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 Injection 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

Buffer: 6.7 mg/mL of [dibasic potassium phosphate](#) in [water](#)

Mobile phase: [Acetonitrile](#) and *Buffer* (52:48). Adjust with 10 N [potassium hydroxide](#) to a pH of 11.0 ± 0.1.

Diluent: [Acetonitrile](#) and [water](#) (52:48)

System suitability solution: 1 mg/mL each of [USP Azaerythromycin A RS](#) and [USP Azithromycin RS](#) in a mixture of [acetonitrile](#) and [water](#) (52:48). Dissolve first in [acetonitrile](#), and then dilute with [water](#) to volume.

Standard solution: 1 mg/mL of [USP Azithromycin RS](#) in a mixture of [acetonitrile](#) and [water](#) (52:48). Dissolve first in [acetonitrile](#), and dilute with [water](#) to volume.

Sample solution: Nominally equivalent to 1 mg/mL of azithromycin from Azithromycin for Injection in *Diluent* prepared as follows. Reconstitute 3 vials individually as directed in the labeling. Mix the contents of all the reconstituted vials. Dilute a portion of the mixture with *Diluent*.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Columns

Guard: 4.6-mm × 1-cm; 5-μm packing [L67](#)

Analytical: 4.6-mm × 15-cm; 5-μm packing [L67](#)

Temperatures

Autosampler: 15°

Column: 40°

Flow rate: 1 mL/min

Injection volume: 15 μL

System suitability

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

[NOTE—The relative retention times for azaerythromycin A and azithromycin are 0.68 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.5 between azaerythromycin A and azithromycin, *System suitability solution*

Tailing factor: NLT 0.9 and NMT 1.5, *Standard solution*

Relative standard deviation: NMT 2%, *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 Azithromycin for Injection 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* (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

- [UNIFORMITY OF DOSAGE UNITS \(905\)](#): Meets the requirements

IMPURITIES

[NOTE—The test for *Limit of Azithromycin N-Oxide, Desosaminylazithromycin, and N-Demethylazithromycin* does not quantify aminoazithromycin, formamido analog, methylformamido analog, and 3'-de(dimethylamino)-3'-oxoazithromycin. If these impurities are part of the impurity profile, the *Limit of Aminoazithromycin, Formamido Analog, Methylformamido Analog, and 3'-De(dimethylamino)-3'-oxoazithromycin* test is recommended in addition to the test for *Limit of Azithromycin N-Oxide, Desosaminylazithromycin, and N-Demethylazithromycin*.]

- **LIMIT OF AZITHROMYCIN N-OXIDE, DESOSAMINYLAZITHROMYCIN, AND N-DEMETHYLAZITHROMYCIN**

Buffer: 3.5 g/L of [dibasic potassium phosphate](#)

Mobile phase: [Acetonitrile](#) and *Buffer* (23:77). Adjust with 5 N [potassium hydroxide](#) to a pH of 10.55 ± 0.05.

Standard stock solution: 0.05 mg/mL of [USP Azithromycin N-oxide RS](#), 45 µg/mL of [USP Desosaminylazithromycin RS](#), and 160 µg/mL each of [USP N-Demethylazithromycin RS](#) and [USP Azithromycin RS](#) in [acetonitrile](#). Sonicate if necessary to dissolve.

Standard solution: 0.001 mg/mL of azithromycin *N-oxide*, 0.9 µg/mL of desosaminylazithromycin, and 3.2 µg/mL each of *N-demethylazithromycin* and azithromycin from *Standard stock solution* in *Mobile phase*

Sample solution: Nominally equivalent to 0.3 mg/mL of azithromycin in *Mobile phase* from Azithromycin for Injection

Chromatographic system

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

Mode: LC

Detector: Amperometric electrochemical

Electrodes: Dual series glassy carbon

Mode: Oxidative screen

Electrode 1: +0.70 ± 0.05 V

Electrode 2: +0.82 ± 0.05 V

Column: 4.6-mm × 15-cm; 3-µm packing [L49](#)

Autosampler temperature: 5°

Flow rate: 1 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

[NOTE—See [Table 1](#) for relative retention times.]

Suitability requirements

Tailing factor: NMT 2.0 for azithromycin and NMT 2.6 for *N-demethylazithromycin*

Relative standard deviation: NMT 10.0% for azithromycin *N-oxide*, desosaminylazithromycin, *N-demethylazithromycin*, and azithromycin

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each specified impurity in the portion of Azithromycin for Injection taken:

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

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

r_S = peak response of each specified impurity from the *Standard solution*

C_S = concentration of the relevant impurity Reference Standard in the *Standard solution* (mg/mL)

C_U = nominal concentration of azithromycin in the *Sample solution* (mg/mL)

P = potency of the relevant Reference Standard (mg/mg)