Clarithromycin for Oral Suspension

DEFINITION
Clarithromycin for Oral Suspension is a dry mixture of Clarithromycin, dispersing agents, diluents, preservatives, and flavorings. It contains NLT 90.0% and NMT 115.0% of the labeled amount of clarithromycin (C_{38}H_{69}NO_{13}), the labeled amount being 25 mg or 50 mg/mL when constituted as directed in the labeling.

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.

ASSAY

Change to read:

• PROCEDURE
Buffer: 0.067 M monobasic potassium phosphate
Mobile phase: Methanol and Buffer (60:40), adjusted with phosphoric acid to a pH of 3.5. Pass through a suitable filter.
Standard stock solution: Equivalent to 2.1 mg/mL of clarithromycin from USP Clarithromycin RS in methanol
Standard solution: 0.415 mg/mL of clarithromycin from Standard stock solution in Mobile phase
Sample stock solution: Constitute the Clarithromycin from Tablets in methanol to a pH of 4.0, and pass through a suitable filter.
Sample solution: Transfer an aliquot of the suspension, equivalent to 1±2 g of clarithromycin, with the aid of 330 mL of Buffer, to a 1000-mL volumetric flask containing 50 mL of Buffer. Shake by mechanical means for 30 min, and dilute with methanol to volume. Sonicate for about 30 min, and allow to cool. Dilute with methanol to volume, add a magnetic stirring bar, and stir for 60 min. Allow to settle, and use the clear supernatant.
Sample solution: Transfer an aliquot of the Sample stock solution, nominally equivalent to 20 mg of clarithromycin, to a 50-mL volumetric flask, dilute with Mobile phase to volume, and pass through a suitable filter.
Chromatographic system
(See Chromatography (621), System Suitability.)
Mode: LC
Detector: UV 210 nm
Columns
Guard (optional): Packing L1
Analytical: 4.6-mm × 15-cm; packing L1
Column temperature: 50°
Flow rate: 1 mL/min
Injection volume: 50 µL
System suitability
Sample: Standard solution
Suitability requirements
Tailing factor: 1.0–1.7
Relative standard deviation: NMT 2.0%
Analysis
Samples: Standard solution and Sample solution
Calculate the percentage of the labeled amount of clarithromycin (C_{38}H_{69}NO_{13}) in the portion of the constituted Clarithromycin for Oral Suspension taken:

\[ \text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_U}{C_S} \right) \times 100 \]

• r_U = peak area response from the Sample solution
• r_S = peak area response from the Standard solution
• C_S = concentration of the Standard solution (mg/mL)
• C_U = nominal concentration of clarithromycin in the Sample solution (mg/mL)

Acceptance criteria: 90.0%–115.0%

PERFORMANCE TESTS
• UNIFORMITY OF DOSAGE UNITS (905) (for powder packaged in single-unit containers): Meets the requirements
• DELIVERABLE VOLUME (698) (for powder packaged in multiple-unit containers): Meets the requirements

SPECIFIC TESTS
• pH (791)
Sample: Use the suspension constituted as directed in the labeling.
Acceptance criteria: 4.0–5.4
• LOSS ON DRYING (731)
Sample: 1 g
Analysis: Dry under vacuum at a pressure not exceeding 5 mm of mercury at 60° for 3 h.
Acceptance criteria: NMT 2.0%

ADDITIONAL REQUIREMENTS
• PACKAGING AND STORAGE: Preserve in tight containers.
• USP REFERENCE STANDARDS (11)
USP Clarithromycin RS

Clarithromycin Tablets

DEFINITION
Clarithromycin Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of C_{38}H_{69}NO_{13}.

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
Mobile phase: Methanol and 0.067 M monobasic potassium phosphate (13:7). Adjust with phosphoric acid to a pH of 4.0, and pass through a suitable filter.
Standard stock solution: 625 µg/mL of clarithromycin from USP Clarithromycin RS dissolved in methanol.
[NOTE—Shake and sonicate to facilitate dissolution.]
Standard solution: 125 µg/mL of clarithromycin from Standard stock solution in Mobile phase. Pass through a suitable filter.
System suitability stock solution: 625 µg/mL of USP Clarithromycin Related Compound A RS from System suitability stock solution in Mobile phase.
Sample stock solution: Equivalent to 4 mg/mL of clarithromycin from finely powdered Tablets in methanol.
[NOTE—Shake by mechanical means for 30 min to disperse and allow any insoluble matter to settle.]
Sample solution: 120 µg/mL of clarithromycin from Sample stock solution in Mobile phase. Pass through a filter of 0.5-µm or finer pore size.
Chromatographic system
(See Chromatography (621), System Suitability.)
Mode: LC
Detector: UV 210 nm
Column: 4.6-mm × 15-cm; packing L1
[NOTE—A guard column containing packing L1 may be added.]
Column temperature: 50°
Flow rate: 1 mL/min
Injection size: 20–50 µL
System suitability
Samples: System suitability solution and Standard solution
Clarithromycin Extended-Release Tablets

DEFINITION
Clarithromycin Extended-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of clarithromycin (C₃₈H₆₉NO₁₃).

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.

ASSAY

Change to read:

• PROCEDURE
Buffer A: 0.067 M monobasic potassium phosphate
Mobile phase: Methanol and Buffer A (13:7). Adjust with phosphoric acid to a pH of 4.0. Pass through a suitable filter.
Standard stock solution: 625 µg/mL of clarithromycin from USP Clarithromycin RS in methanol. Shake and sonicate, if necessary, to facilitate dissolution.
Standard solution: 125 µg/mL of clarithromycin in Mobile phase from Standard stock solution. Pass through a suitable filter.
System suitability stock solution: 625 µg/mL of USP Clarithromycin Related Compound A RS in methanol
System suitability solution: 125 µg/mL of USP Clarithromycin Related Compound A RS from System suitability stock solution and 125 µg/mL of clarithromycin from Standard stock solution in Mobile phase.
Sample stock solution: Transfer nominally 2000 mg of clarithromycin from finely powdered Tablets to a 500-mL volumetric flask with the aid of methanol. Add about 350 mL of methanol, and shake by mechanical means for 30 min. Dilute with methanol to volume, and sonicate for 30 min. Cool to room temperature, and allow to stand for at least 16 h. Mix, allow any insoluble matter to settle, and use the supernatant.
Sample solution: Transfer 3.0 mL of the Sample stock solution to a 100-mL volumetric flask, and dilute with Mobile phase to volume. Pass through a suitable filter.

Chromatographic system
(See Chromatography (621), System Suitability.)
Mode: LC
Detector: UV 210 nm
Columns
Guard (optional): Packing L1
Analytical: 4.6-mm × 15-cm; packing L1
Column temperature: 50°
Flow rate: 1 mL/min
Injection volume: 20–50 µL
System suitability
Samples: Standard solution and System suitability solution

[NOTE—The relative retention times for clarithromycin and clarithromycin related compound A are 0.75 and 1.0, respectively.]