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 for Oral Suspension as directed in the labeling. 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 ▲*USP36*
Tailing factor: 1.0–1.7
▲*USP36*
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:

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

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 in methanol.
System suitability solution: 125 µg/mL of USP Clarithromycin RS from *Standard stock solution* and 125 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*

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

Suitability requirements

Resolution: NLT 2.0 between clarithromycin and clarithromycin related compound A, *System suitability solution*

Column efficiency: NLT 750 theoretical plates from the clarithromycin peak, *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 percentage of label claim of $C_{38}H_{69}NO_{13}$ in the portion of Tablets taken:

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **DISSOLUTION** ⟨**711**⟩

Buffer solution: Prepare a solution containing 13.61 mg/mL of sodium acetate trihydrate in water. Prepare another solution by diluting 5.7 mL of glacial acetic acid to 1 L with water. Combine portions of the two solutions to obtain a pH of 5.0.

Medium: *Buffer solution*, 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Standard solution: Proceed as directed in the *Assay*.

Sample solution: Dilute with *Mobile phase* to yield a nominal concentration of 125 µg/mL of clarithromycin.

Mobile phase, System suitability solution, Chromatographic system, and **System suitability:** Proceed as directed for *Assay*.

Analysis

Samples: *Standard solution* and *Sample solution*

Determine the amount of $C_{38}H_{69}NO_{13}$ dissolved in the *Medium*, as directed in the *Assay*.

Calculate the percentage of clarithromycin dissolved:

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

r_U = peak area of the *Sample solution*
r_S = peak area of the *Standard solution*
C_S = concentration of the *Standard solution* (µg/mL)
C_U = nominal concentration of the *Sample solution* (µg/mL)

Tolerances: NLT 80% (Q) of the labeled amount of $C_{38}H_{69}NO_{13}$ is dissolved.

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

SPECIFIC TESTS

• **LOSS ON DRYING** ⟨**731**⟩**:** Dry a portion of powdered Tablets in vacuum at a pressure not exceeding 5 mm of mercury at 110° for 3 h: it loses NMT 6.0% of its weight.

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in tight containers.

• **USP REFERENCE STANDARDS** ⟨**11**⟩

USP Clarithromycin RS

USP Clarithromycin Related Compound A RS

6,11-Di-*O*-methylerythromycin A.

$C_{39}H_{71}NO_{13}$ 762.00

Clarithromycin Extended-Release Tablets

DEFINITION

Clarithromycin Extended-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of clarithromycin ($C_{38}H_{69}NO_{13}$).

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 about 0.75 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between clarithromycin and clarithromycin related compound A, *System suitability solution*

▲▲*USP36*

Tailing factor: 0.9–1.5, *Standard solution*

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