Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-Aug-2016
Document Type: USP Monographs
DocId: GUID-2066A25D-F5B5-4274-911B-5A6EF3A31C62_1_en-US
DOI: https://doi.org/10.31003/USPNF_M17995_01_01
DOI Ref: 4ua05

Clarithromycin Tablets

DEFINITION
Clarithromycin 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
• **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.

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 the *Standard stock solution* and 125 µg/mL of USP Clarithromycin Related Compound A RS from the *System suitability stock solution* in *Mobile phase*

Standard stock solution: 625 µg/mL of clarithromycin from USP Clarithromycin RS dissolved in methanol. 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.

Sample stock solution: Nominally 4 mg/mL of clarithromycin from finely powdered Tablets in methanol. Shake by mechanical means for 30 min to disperse, and allow any insoluble matter to settle.

Sample solution: 120 µg/mL of clarithromycin from the *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; 5-µm packing L1

[Note—A guard column containing packing L1 may be added.]

Column temperature: 50°

Flow rate: 1 mL/min

Injection volume: 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*

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 clarithromycin ($C_{38}H_{69}NO_{13}$) 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: 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 with water to 1 L. Combine portions of the two solutions to obtain a pH of 5.0.

Medium: *Buffer*, 900 mL

Apparatus 2: 50 rpm

Time: 30 min

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

Standard stock solution: 625 µg/mL of clarithromycin from USP Clarithromycin RS dissolved in *Buffer*. Shake, and sonicate to facilitate dissolution.

Standard solution: 125 µg/mL of clarithromycin from the *Standard stock solution* in *Mobile phase*. Pass through a suitable filter.

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of clarithromycin ($C_{38}H_{69}NO_{13}$) dissolved:

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

r_U = peak area from the *Sample solution*

r_S = peak area from 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 clarithromycin ($C_{38}H_{69}NO_{13}$) is dissolved.

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

IMPURITIES

• **Organic Impurities**

Solution A: 4.76 g/L of monobasic potassium phosphate adjusted with dilute phosphoric acid (1 in 10) or 4.5% (w/v) of potassium hydroxide to a pH of 4.4

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	75	25
32	40	60
34	40	60
36	75	25
42	75	25

Diluent: Acetonitrile and water (1:1)

System suitability solution: 1.5 mg/mL of USP Clarithromycin Identity RS in acetonitrile and water (1:1). Dissolve first in acetonitrile, using 50% of the final volume, and dilute with water to volume.

Standard stock solution: 1.5 mg/mL of USP Clarithromycin RS in acetonitrile and water (1:1). Dissolve first in acetonitrile, using 50% of the final volume, and dilute with water to volume.

Standard solution 1: 0.075 mg/mL of USP Clarithromycin RS from *Standard stock solution* in *Diluent*

Standard solution 2: 0.0075 mg/mL of USP Clarithromycin RS from *Standard solution 1* in *Diluent*

Sample solution: Nominally 1.5 mg/mL of clarithromycin from finely powdered Tablets in acetonitrile and water (1:1). Dissolve first in acetonitrile, using 50% of the final volume, and dilute with water to volume. Sonicate, and pass through a suitable filter.

Chromatographic system

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

Mode: LC

Detector: UV 205 nm

Column: 4.6-mm × 10-cm; 3.5-µm packing L1

Column temperature: 40°

Flow rate: 1.1 mL/min

Injection volume: 10 µL

System suitability

Samples: *System suitability solution* and *Standard solution 1*

[NOTE—See *Table 2* for relative retention times. The typical retention time for clarithromycin is about 11 min.]

Suitability requirements

Peak-to-valley ratio: NLT 3.0 between clarithromycin and clarithromycin impurity D, *System suitability solution*. Calculate as follows:

$$\text{Result} = H_P/H_V$$

H_P = height above the baseline of the clarithromycin impurity D peak

H_V = height above the baseline of the lowest point of the curve separating the clarithromycin impurity D peak from the clarithromycin peak

Tailing factor: NMT 1.7, *Standard solution 1*

Analysis

Samples: *Standard solution 2* and *Sample solution*

Calculate the percentage of each impurity in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from *Standard solution 2*

C_S = concentration of clarithromycin in *Standard solution 2* (mg/mL)

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

F = relative response factor (see *Table 2*)

Acceptance criteria: The reporting threshold is 0.1%.Disregard the peaks eluting before impurity I and after impurity H.

Any individual impurity: NMT 1.0%; NMT four impurities exceed 0.4%.

Total impurities: NMT 3.5%

Table 2

Name	Relative Retention Time	Relative Response Factor
Clarithromycin impurity I[a]	0.38	1.0
Clarithromycin impurity A[b] (clarithromycin F)	0.42	1.0

Name	Relative Retention Time	Relative Response Factor
Clarithromycin impurity J[c]	0.63	1.0
Clarithromycin impurity L[d]	0.74	1.0
Clarithromycin impurity B[e]	0.79	1.0
Clarithromycin impurity M[f]	0.81	1.0
Clarithromycin impurity C[g]	0.89	1.0
Clarithromycin impurity D[h]	0.96	1.0
Clarithromycin	1.0	—
Clarithromycin impurity N[i]	1.15	1.0
Clarithromycin related compound A[j]	1.27	1.0
Clarithromycin impurity F[k]	1.33	1.0
Clarithromycin impurity P[l]	1.35	1.0
Clarithromycin impurity O[m]	1.38	1.0
Clarithromycin impurity K[n]	1.59	1.0
Clarithromycin impurity G[o]	1.72	3.7
Clarithromycin impurity H[p]	1.82	6.7

[a] 3-*O*-Decladinosyl-6-*O*-methylerythromycin A.

[b] 2-Demethyl-2-(hydroxymethyl)-6-*O*-methylerythromycin A.

[c] Erythromycin A (*E*)-9-oxime.

[d] 6-*O*-Methylerythromycin (*Z*)-9-oxime.

[e] 6-*O*-Methyl-15-norerythromycin A.

[f] 3"-*N*-Demethyl-6-*O*-methylerythromycin A (*E*)-9-oxime.

[g] 6-*O*-Methylerythromycin A (*E*)-9-oxime.

[h] 3"-*N*-Demethyl-6-*O*-methylerythromycin A.

[i] (10*E*)-10,11-Didehydro-11-deoxy-6-*O*-methylerythromycin A.

[j] 6,11-Di-*O*-methylerythromycin A.

[k] 6,12-Di-*O*-methylerythromycin A.

[l] 4',6-Di-*O*-methylerythromycin A.

[m] 6-*O*-Methylerythromycin A (*Z*)-9-(*O*-methyloxime).

[n] (1*S*,2*R*,5*R*,6*S*,7*S*,8*R*,9*R*,11*Z*)-2-Ethyl-6-hydroxy-9-methoxy-1,5,7,9,11,13-hexamethyl-8-[[3,4,6-trideoxy-3-(dimethylamino)-β-D-*xylo*-hexapyranosyl]oxy]-3,15-dioxabicyclo[10.2.1]pentadeca-11,13-dien-4-one (3-*O*-decladinosyl-8,9:10,11-dianhydro-6-*O*-methylerythromycin A)-9,12-hemiketal.

[o] 6-*O*-Methylerythromycin A (*E*)-9-(*O*-methyloxime).

p 3"-*N*-Demethyl-3"-*N*-formyl-6-*O*-methylerythromycin A.

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

Analysis: Dry a portion of powdered Tablets under vacuum at a pressure not exceeding 5 mm of mercury at 110° for 3 h.

Acceptance criteria: NMT 6.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.

• **USP Reference Standards** ⟨11⟩

USP Clarithromycin RS

USP Clarithromycin Identity RS

This is a mixture of clarithromycin, clarithromycin impurity D (3"-*N*-demethyl-6-*O*-methylerythromycin A; $C_{37}H_{67}NO_{13}$ 733.9), and other impurities.

USP Clarithromycin Related Compound A RS

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

$C_{39}H_{71}NO_{13}$ 761.98

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

Topic/Question	Contact	Expert Committee
CLARITHROMYCIN TABLETS	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 46(2)

Current DocID: GUID-2066A25D-F5B5-4274-911B-5A6EF3A31C62_1_en-US

DOI: https://doi.org/10.31003/USPNF_M17995_01_01

DOI ref: 4ua05