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Amoxicillin and Clavulanate Potassium Tablets

DEFINITION

Amoxicillin and Clavulanate Potassium Tablets contain the equivalent of NLT 90.0% and NMT 120.0% of the labeled amounts of amoxicillin ($C_{16}H_{19}N_3O_5S$) and clavulanic acid ($C_8H_9NO_5$).

IDENTIFICATION

The retention times of the major peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Buffer: 7.8 g of monobasic sodium phosphate in 900 mL of water. Adjust with phosphoric acid or 10 N sodium hydroxide to a pH of 4.4 ± 0.1, and dilute with water to 1000 mL.

Mobile phase: Methanol and *Buffer* (1:19). Pass through a suitable filter.

Standard solution: 0.5 mg/mL of USP Amoxicillin RS and 0.2 mg/mL of USP Clavulanate Lithium RS in water

Sample stock solution: Dissolve NLT 10 Tablets in water with the aid of mechanical stirring. Transfer to a suitable volumetric flask, and dilute with water to volume.

Sample solution: Dilute a suitable volume of the *Sample stock solution* with water to obtain a solution containing 0.5 mg/mL of amoxicillin. [Note—Use the *Sample solution* within 1 h.]

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4-mm × 30-cm; 3- to 10-µm packing L1

Flow rate: 2 mL/min

Injection size: 20 µL

System suitability

Sample: *Standard solution*

[Note—The relative retention times for clavulanic acid and amoxicillin are 0.5 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 3.5 between the amoxicillin and clavulanic acid peaks

Tailing factor: NMT 1.5 for each analyte peak

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{16}H_{19}N_3O_5S$ in each Tablet taken:

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

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

r_S = peak response of amoxicillin from the *Standard solution*

C_S = concentration of USP Amoxicillin RS in the *Standard solution* (mg/mL)

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

P = potency of USP Amoxicillin RS (µg/mg)

F = conversion factor, 0.001 mg/µg

Calculate the percentage of $C_8H_9NO_5$ in each Tablet taken:

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

r_U = peak response of clavulanic acid from the *Sample solution*

r_S = peak response of clavulanic acid from the *Standard solution*

C_S = concentration of USP Clavulanate Lithium RS in the *Standard solution* (mg/mL)

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

P = potency of clavulanic acid in USP Clavulanate Lithium RS (mg/mg)

Acceptance criteria: 90.0%–120.0%

PERFORMANCE TESTS

• **Disintegration ⟨701⟩:** Tablets labeled for veterinary use only; 30 min, simulated gastric fluid TS being substituted for water in the test

• **Dissolution ⟨711⟩**

[Note—Tablets labeled for veterinary use only are exempt from this requirement.]

Test 1

Medium: Water; 900 mL

Apparatus 2: 75 rpm

Time: 30 min; or 45 min where the Tablets are labeled as chewable

Analysis: Determine the amount of $C_{16}H_{19}N_3O_5S$ and $C_8H_9NO_5$ dissolved, using the *Analysis* set forth in the *Assay*, making any necessary volumetric adjustments.

Tolerances: NLT 85% (Q) of the labeled amount of $C_{16}H_{19}N_3O_5S$ and NLT 80% (Q) of the labeled amount of $C_8H_9NO_5$ are dissolved.

For Tablets labeled as chewable: NLT 80% (Q) of the labeled amounts of $C_{16}H_{19}N_3O_5S$ and $C_8H_9NO_5$ is dissolved in 45 min.

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

Medium, Apparatus 2, and **Analysis:** Proceed as directed for *Test 1*.

Times: 45 min for amoxicillin, and 30 min for clavulanic acid

Tolerances: NLT 85% (Q) of the labeled amount of $C_{16}H_{19}N_3O_5S$ and NLT 80% (Q) of the labeled amount of $C_8H_9NO_5$ are dissolved.

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

SPECIFIC TESTS

• **Water Determination,** *Method I* **⟨921⟩:**

Tablet Label Claim Amoxicillin (mg/Tablet)	Acceptance Criteria, NMT (%)
≤250	7.5
>250 and ≤500	10.0
>500	11.0

For products labeled as chewable Tablets:

Tablet Label Claim Amoxicillin (mg/Tablet)	Acceptance Criteria, NMT (%)
≤125	6.0
>125	8.0

For Tablets labeled for veterinary use only: NMT 10.0%

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** The total aerobic microbial count does not exceed 10^3 cfu/g, and the total combined molds and yeasts count does not exceed 10^2 cfu/g.

ADDITIONAL REQUIREMENTS

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

• **Labeling:** Label chewable Tablets to include the word “chewable” in juxtaposition to the official name. The labeling indicates that chewable Tablets may be chewed before being swallowed or may be swallowed whole. Tablets intended for veterinary use only are so labeled. When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.

• **USP Reference Standards ⟨11⟩**

USP Amoxicillin RS

USP Clavulanate Lithium RS

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

Topic/Question	Contact	Expert Committee
AMOXICILLIN AND CLAVULANATE POTASSIUM TABLETS	Documentary Standards Support	SM12020 Small Molecules 1

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