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Cyclophosphamide Tablets

DEFINITION

Cyclophosphamide Tablets contain Cyclophosphamide equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of anhydrous cyclophosphamide ($C_7H_{15}Cl_2N_2O_2P$).

IDENTIFICATION

Change to read:

• **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020)

Sample: Extract a portion of finely powdered Tablets, equivalent to 50 mg of cyclophosphamide, with 25 mL of chloroform. Filter about 2 mL of the chloroform solution, mix the filtrate with 500 mg of potassium bromide, evaporate the chloroform, carefully removing the last trace of solvent in a small vacuum flask, and use the residue to prepare a potassium bromide dispersion.

Acceptance criteria: The IR absorption spectrum of the *Sample* exhibits maxima, between 6.5 and 14 µm, only at the same wavelengths as those of a similar preparation of USP Cyclophosphamide RS.

• **B.** 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: Acetonitrile and water (30:70)

Ethylparaben solution: Dissolve 185 mg of ethylparaben in 250 mL of alcohol in a 1000-mL volumetric flask, and dilute with water to volume.

System suitability solution: 0.5 mg/mL of USP Cyclophosphamide RS and 0.0185 mg/mL of ethylparaben in water prepared as follows. Transfer a quantity of USP Cyclophosphamide RS to a suitable volumetric flask, add water equivalent to 50% of the final volume, and shake to dissolve. Add *Ethylparaben solution* equivalent to 10% of the final volume, and dilute with water to volume.

Standard solution: 0.5 mg/mL of USP Cyclophosphamide RS in water

Sample solution: Nominally equivalent to 0.5 mg/mL of anhydrous cyclophosphamide prepared as follows. Transfer NLT 10 Tablets to a suitable volumetric flask. Fill about half full with water, shake for 30 min, and dilute with water to volume. Pass through fast, fluted filter paper, and discard the first 40–50 mL of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 195 nm

Column: 3.9-mm × 30-cm; packing L1

Flow rate: 1.5 mL/min

Injection volume: 25 µL

System suitability

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

[Note—The relative retention times for cyclophosphamide and ethylparaben are 0.7 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2 between cyclophosphamide and ethylparaben, *System suitability solution*

Relative standard deviation: NMT 2% from six replicate injections, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of anhydrous cyclophosphamide ($C_7H_{15}Cl_2N_2O_2P$) in the portion of Tablets taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: Water; 900 mL, deaerated

Apparatus 1: 100 rpm

Time: 45 min

Mobile phase: Acetonitrile and water (30:70)

Standard solution: USP Cyclophosphamide RS in water at a concentration similar to that of the *Sample solution*

Sample solution: Pass a portion of solution under test through a suitable filter of 0.8-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 195 nm

Column: 3.9-mm × 30-cm; packing L1

Flow rate: 1.5 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of anhydrous cyclophosphamide ($C_7H_{15}Cl_2N_2O_2P$) dissolved:

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

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

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

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances: NLT 75% (Q) of the labeled amount of anhydrous cyclophosphamide ($C_7H_{15}Cl_2N_2O_2P$) is dissolved.

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

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers. Storage at a temperature not exceeding 25° is recommended. Tablets will withstand brief exposure to temperatures up to 30° but are to be protected from temperatures above 30°.

• **USP Reference Standards ⟨11⟩**

USP Cyclophosphamide RS

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

Topic/Question	Contact	Expert Committee
CYCLOPHOSPHAMIDE TABLETS	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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