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Chlorambucil Tablets

DEFINITION
Chlorambucil Tablets contain NLT 85.0% and NMT 110.0% of the labeled amount of chlorambucil ($C_{14}H_{19}Cl_2NO_2$).

IDENTIFICATION

Change to read:

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

Sample solution: Shake a quantity of finely powdered Tablets, equivalent to 16 mg of chlorambucil, with 20 mL of carbon disulfide. Filter, evaporate to dryness, and dissolve the residue in 2 mL of carbon disulfide.

Cell: 1 mm

Acceptance criteria: Meet the requirements

ASSAY

• **Procedure**

Mobile phase: Mix 500 mL of alcohol with 1.0 mL of glacial acetic acid. Dilute with water to 1 L. Degas the solution at a pressure of approximately 250 mm of mercury for 2 min. [Note—The alcohol concentration may be varied to meet system suitability requirements and to provide a suitable elution time for chlorambucil.]

Internal standard solution: 0.4 mg/mL of USP Propylparaben RS in alcohol

Standard stock solution: 1 mg/mL of USP Chlorambucil RS in alcohol

Standard solution: 0.02 mg/mL of USP Chlorambucil RS in alcohol prepared as follows. Transfer 2.0 mL of the *Standard stock solution* into a 100-mL volumetric flask containing 50 mL of alcohol and, while gently swirling, add 5.0 mL of 0.1 N hydrochloric acid and 2.0 mL of *Internal standard solution*. Dilute with alcohol to volume.

Sample solution: Nominally 0.02 mg/mL of chlorambucil in alcohol prepared as follows. Transfer finely powdered Tablets (NLT 20), equivalent to 2 mg of chlorambucil, into a 100-mL volumetric flask containing 50 mL of alcohol and, while gently swirling, add 5.0 mL of 0.1 N hydrochloric acid and 2.0 mL of *Internal standard solution*. Sonicate for 5 min, and dilute with alcohol to volume. Filter through a medium pore size, sintered-glass filtering funnel, maintaining reduced pressure for the minimum necessary time to avoid solvent loss from evaporation.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 25- or 30-cm × 2-mm; 5- to 10-µm packing L1

Flow rate: Capable of giving the required *Resolution* in *Suitability requirements* and a suitable elution time

Injection volume: 10–12 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between the propylparaben and chlorambucil peaks

Relative standard deviation: NMT 2.0% for 6–8 injections, for the peak response ratio of chlorambucil to propylparaben

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of chlorambucil ($C_{14}H_{19}Cl_2NO_2$) in the portion of Tablets taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = peak response ratio of chlorambucil to propylparaben from the *Sample solution*

R_S = peak response ratio of chlorambucil to propylparaben from the *Standard solution*

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

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

Acceptance criteria: 85.0%–110.0%

PERFORMANCE TESTS

• **Disintegration ⟨701⟩**

Analysis: Place 1 Tablet in each of the six tubes of the basket, and if the Tablet has a soluble external coating, immerse the basket in water at room temperature for 5 min. Operate the apparatus, using simulated gastric fluid TS maintained at 37 ± 2° as the immersion fluid. After 30 min of operation in simulated gastric fluid TS, lift the basket from the fluid, and observe the Tablets. If the Tablets have not disintegrated completely, substitute simulated intestinal fluid TS maintained at 37 ± 2° as the immersion fluid, and continue the test for a total period of time equal to 45 min, including previous exposure to water and simulated gastric fluid TS. Lift the basket from the fluid, and observe the Tablets.

Acceptance criteria: All of the Tablets have disintegrated completely. If 1 or 2 Tablets fail to disintegrate completely, repeat the test on 12 additional Tablets: NLT 16 of the total of 18 Tablets tested disintegrate completely.

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

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve coated Tablets in well-closed containers. Preserve uncoated Tablets in well-closed, light-resistant containers.

• **USP Reference Standards ⟨11⟩**

USP Chlorambucil RS

USP Propylparaben RS

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

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

Chromatographic Database Information: Chromatographic Database

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