

Chlorpromazine Hydrochloride Tablets

Type of Posting	Revision Bulletin
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Expert Committee	Small Molecules 4
Reason for Revision	Compliance

In accordance with the Rules and Procedures of the 2020–2025 Council of Experts, the Small Molecules 4 Expert Committee has revised the Chlorpromazine Hydrochloride Tablets monograph. The purpose for the revision is to add *Dissolution Test 2* to accommodate FDA-approved drug products which have different dissolution conditions. Labeling information has also been added to support the inclusion of *Dissolution Test 2*. Additionally, minor editorial changes have been made to update the monograph to current *USP* style.

The Chlorpromazine Hydrochloride Tablets Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Heather Joyce, Team Lead–Senior Scientific Liaison (301-998-6792 or hrj@usp.org).

Chlorpromazine Hydrochloride Tablets

DEFINITION

Chlorpromazine Hydrochloride Tablets contain NLT 95.0% and NMT 105.0% of the labeled amount of chlorpromazine hydrochloride ($C_{17}H_{19}ClN_2S \cdot HCl$).

[NOTE—Throughout the following analyses, protect sample specimens, the Reference Standard, and solutions containing them, by conducting the procedures without delay, under subdued light, or using low-actinic glassware.]

IDENTIFICATION

• **A.** The principal spot found in the test for *Other Alkylated Phenothiazines* corresponds in R_f to the spot of the *Standard solution*.

• **B. IDENTIFICATION TESTS—GENERAL (191), Chloride**

Sample stock solution: Digest a quantity of powdered Tablets, equivalent to about 25 mg of chlorpromazine hydrochloride, with 25 mL of [water](#). Pass the resulting solution through a suitable filter.

Sample solution: A solution (1 in 10) using the *Sample stock solution*

Acceptance criteria: Meets the requirements

ASSAY

Change to read:

PROCEDURE

Standard solution: 8 $\mu\text{g/mL}$ of [USP Chlorpromazine Hydrochloride RS](#) in 0.1 N [hydrochloric acid](#)

Sample stock solution: Nominally 0.2 mg/mL of chlorpromazine hydrochloride prepared as follows.

Transfer a portion of finely powdered Tablets (NLT 20), equivalent to 100 mg of chlorpromazine hydrochloride, to a 500-mL volumetric flask. Add 200 mL of [water](#) and 5 mL of [hydrochloric acid](#), insert the stopper, and shake for about 10 min. Dilute with [water](#) to volume, and mix. Pass a portion of the resulting solution through a suitable filter, discarding the first 50 mL of the filtrate.

Sample solution: Nominally 8 $\mu\text{g/mL}$ of chlorpromazine hydrochloride prepared as follows. Pipet 10.0 mL of the *Sample stock solution* into a 250-mL separator, add 20 mL of [water](#), render alkaline with [ammonium hydroxide](#), and extract with four 25-mL portions of [ethyl ether](#).[▲] (RB 16-Sep-2020) Extract the combined [ethyl ether](#).[▲] (RB 16-Sep-2020) extracts with four 25-mL portions of 0.1 N [hydrochloric acid](#), collecting the aqueous extracts in a 250-mL volumetric flask. Aerate to remove residual [ethyl ether](#).[▲] (RB 16-Sep-2020) and dilute with 0.1 N [hydrochloric acid](#) to volume.

Instrumental conditions

Mode: UV-Vis

Analytical wavelengths: 254 and 277 nm

Cell: 1 cm

Blank: 0.1 N [hydrochloric acid](#)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of chlorpromazine hydrochloride ($C_{17}H_{19}ClN_2S \cdot HCl$) in the portion of Tablets taken:

$$\text{Result} = [(A_{U1} - A_{U2}) / (A_{S1} - A_{S2})] \times (C_S / C_U) \times 100$$

A_{U1} = absorbance of the *Sample solution*, 254 nm

A_{U2} = absorbance of the *Sample solution*, 277 nm

A_{S1} = absorbance of the *Standard solution*, 254 nm

A_{S2} = absorbance of the *Standard solution*, 277 nm

C_S = concentration of [USP Chlorpromazine Hydrochloride RS](#) in the *Standard solution* ($\mu\text{g/mL}$)

C_U = nominal concentration of chlorpromazine hydrochloride in the *Sample solution* ($\mu\text{g/mL}$)

Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS

Change to read:

• [DISSOLUTION \(711\)](#)

▲ **Test 1** ▲ (RB 16-Sep-2020)

Medium: 0.1 N [hydrochloric acid](#) solution; 900 mL

Apparatus 1: 50 rpm

Time: 30 min

Standard solution: [USP Chlorpromazine Hydrochloride RS](#) in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter. Dilute with *Medium*, if necessary.

Instrumental conditions

Mode: UV-Vis

Analytical wavelength: Maximum absorbance at about 254 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Determine the percentage of the labeled amount of chlorpromazine hydrochloride ($\text{C}_{17}\text{H}_{19}\text{ClN}_2\text{S} \cdot \text{HCl}$) dissolved.

Tolerances: NLT 80% (Q) of the labeled amount of chlorpromazine hydrochloride ($\text{C}_{17}\text{H}_{19}\text{ClN}_2\text{S} \cdot \text{HCl}$) is dissolved.

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

Medium: 0.1 N [hydrochloric acid](#) solution; 500 mL, deaerated

Apparatus 1: 75 rpm

Time: 15 min

Standard solution: 0.055 mg/mL of [USP Chlorpromazine Hydrochloride RS](#) in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter. Dilute with *Medium*, if necessary.

Instrumental conditions

(See [Ultraviolet-Visible Spectroscopy \(857\)](#).)

Mode: UV-Vis

Analytical wavelength: UV 254 nm

Cell: 1.0 mm

Blank: *Medium*

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of chlorpromazine hydrochloride ($C_{17}H_{19}ClN_2S \cdot HCl$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times D \times (1/L) \times 100$$

A_U = absorbance of chlorpromazine from the *Sample solution*

A_S = absorbance of chlorpromazine from the *Standard solution*

C_S = concentration of [USP Chlorpromazine Hydrochloride RS](#) in the *Standard solution* ($\mu\text{g/mL}$)

V = volume of *Medium*, 500 mL

D = dilution factor for the *Sample solution*

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of chlorpromazine hydrochloride ($C_{17}H_{19}ClN_2S \cdot HCl$) is dissolved. ▲ (RB 16-Sep-2020)

- **UNIFORMITY OF DOSAGE UNITS** (905): Meet the requirements

IMPURITIES

Change to read:

- **OTHER ALKYLATED PHENOTHAZINES**

Solution A: [Ethyl acetate](#) saturated with [ammonium hydroxide](#)

Standard stock solution: 5 mg/mL of [USP Chlorpromazine Hydrochloride RS](#) in [methanol](#)

Standard solution: 25 $\mu\text{g/mL}$ from *Standard stock solution* in [methanol](#)

Sample solution: Transfer a portion of finely powdered Tablets, equivalent to 50 mg of chlorpromazine hydrochloride, to a stoppered centrifuge tube. Add 10 mL of [methanol](#), shake vigorously, and centrifuge. Prior washing with [water](#) may be used to remove any sugar coating.

Chromatographic system

Mode: TLC

Adsorbent: Chromatographic silica gel mixture

Application volume: 10 μL

Developing solvent system: Freshly prepared mixture of ▲ [ethyl ether](#) ▲ (RB 16-Sep-2020) and *Solution A* (50:50)

Analysis

Samples: *Standard stock solution*, *Standard solution*, and *Sample solution*

Apply separately the *Standard stock solution*, *Standard solution*, and *Sample solution* to the starting line of a thin-layer chromatographic plate coated with *Adsorbent*. Develop the chromatogram, using the *Developing solvent system*, until the solvent front has moved about 10 cm from the origin. Remove the plate from the chamber, and air-dry for 20 min. View under short-wave UV light.

Acceptance criteria: The area and intensity of any spot, other than the principal spot, from the *Sample solution* is not greater than that of the spot of the *Standard solution* (0.5%).

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed, light-resistant containers.

Add the following:

- ▲ **LABELING:** The labeling states the *Dissolution* test used only if *Test 1* is not used. ▲ (RB 16-Sep-2020)
- **USP REFERENCE STANDARDS** (11)
[USP Chlorpromazine Hydrochloride RS](#)

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