Chlorpromazine Hydrochloride Tablets

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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 (C₁₇H₁₉ClN₂S · 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 µg/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 µg/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. Extract the combined 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, 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 (C₁₇H₁₉ClN₂S · HCl) in the portion of Tablets taken:

\[
\text{Result} = \left[ \frac{(A_{U1} - A_{U2})/(A_{S1} - A_{S2})}{(C_S/C_U)} \right] \times 100
\]
\[ A_{U1} = \text{absorbance of the Sample solution, 254 nm} \]
\[ A_{U2} = \text{absorbance of the Sample solution, 277 nm} \]
\[ A_{S1} = \text{absorbance of the Standard solution, 254 nm} \]
\[ A_{S2} = \text{absorbance of the Standard solution, 277 nm} \]
\[ C_s = \text{concentration of USP Chlorpromazine Hydrochloride RS in the Standard solution (µg/mL)} \]
\[ C_u = \text{nominal concentration of chlorpromazine hydrochloride in the Sample solution (µg/mL)} \]

Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS

**Change to read:**

- **Dissolution** *(711)*

\[ ^A \text{Test 1} \] *(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.

\[ ^A \text{Test 2} \] 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 \( \left( C_{17}H_{19}ClN_2S \cdot HCl \right) \) dissolved:

\[
\text{Result} = \left( \frac{A_U}{A_S} \right) \times C_S \times V \times D \times \left( \frac{1}{L} \right) \times 100
\]

- \( A_U \) = 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* (µg/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 \( \left( C_{17}H_{19}ClN_2S \cdot HCl \right) \) is dissolved.▲ (RB 16-Sep-2020)

- **Uniformity of Dosage Units** (905): Meet the requirements

**IMPURITIES**

*Change to read:*

- **Other Alkylated Phenothiazines**
- **Solution A:** *Ethyl acetate* saturated with *ammonium hydroxide*
- **Standard stock solution:** 5 mg/mL of *USP Chlorpromazine Hydrochloride RS* in *methanol*
- **Standard solution:** 25 µg/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*