

## Chlorpromazine Hydrochloride Tablets

<b>Type of Posting</b>	Notice of Intent to Revise
<b>Posting Date</b>	31–July–2020
<b>Targeted Official Date</b>	To Be Determined, Revision Bulletin
<b>Expert Committee</b>	Chemical Medicines Monographs 4

In accordance with section 7.04 (c) of the 2015–2020 Rules and Procedures of the Council of Experts and the [Pending Monograph Guideline](#), this is to provide notice that the Chemical Medicines Monographs 4 Expert Committee intends to revise the Chlorpromazine Hydrochloride Tablets monograph.

Based on the supporting data received from manufacturers awaiting FDA approval, the Expert Committee proposes to add *Dissolution Test 2* to accommodate FDA-approved drug products which have different dissolution conditions.

*Labeling* information has been added to support the inclusion of *Dissolution Test 2*.

Existing references to reagents have been updated for consistency with the reagent entry names. For additional information about reagent cross references, please see the related [Compendial Notice](#).

Additionally, minor editorial changes have been made to update the monograph to current *USP* style.

The proposed revision is contingent on FDA approval of a product that meets the proposed monograph specifications. The proposed revision will be published as a Revision Bulletin and an official date will be assigned to coincide as closely as possible with the FDA approval of the associated product.

See below for additional information about the proposed text.<sup>1</sup>

Should you have any questions, please contact Heather Joyce, Senior Scientific Liaison to the Chemical Medicines Monographs 4 Expert Committee (301-998-6792 or [hrj@usp.org](mailto:hrj@usp.org)).

---

<sup>1</sup> This text is not the official version of a *USP–NF* monograph and may not reflect the full and accurate contents of the currently official monograph. Please refer to the current edition of the *USP–NF* for official text.

USP provides this text to indicate changes that we anticipate will be made official once the product subject to this proposed revision under the Pending Monograph Program receives FDA approval. Once FDA approval is granted for the associated revision request, a Revision Bulletin will be posted that will include the changes indicated herein, as well as any changes indicated in the product's final approval, combined with the text of the monograph as effective on the date of approval. Any revisions made to a monograph under the Pending Monograph Program that are posted without prior publication for comment in the *Pharmacopeial Forum* must also meet the requirements outlined in the [USP Guideline on Use of Accelerated Processes for Revisions to the USP–NF](#).

# 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](#).  $\blacktriangle$  (TBD) Extract the combined [ethyl ether](#)  $\blacktriangle$  (TBD) 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](#),  $\blacktriangle$  (TBD) 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

= absorbance of the *Standard solution*, 277 nm

$A_{S2}$

$C_S$  = 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** ▲ (TBD)

**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 ( $\text{C}_{17}\text{H}_{19}\text{ClN}_2\text{S} \cdot \text{HCl}$ ) 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 ( $\text{C}_{17}\text{H}_{19}\text{ClN}_2\text{S} \cdot \text{HCl}$ ) is dissolved. ▲ (TBD)

- **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  $\mu\text{g/mL}$  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  $\mu\text{L}$

**Developing solvent system:** Freshly prepared mixture of ▲ [ethyl ether](#) ▲ (TBD) 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. ▲ (TBD)

- **USP REFERENCE STANDARDS** (11)

[USP Chlorpromazine Hydrochloride RS](#)

---

### Page Information:

Not Applicable

### DocID:

© The United States Pharmacopeial Convention *All Rights Reserved*.