Chlorpromazine Hydrochloride Tablets

Type of Posting	Notice of Intent to Revise
Posting Date	26-Jan-2024
Targeted Official Date	To Be Determined, Revision Bulletin
Expert Committee	Small Molecules 4

In accordance with the Rules and Procedures of the Council of Experts and the Pending Monograph Guideline, this is to provide notice that the Small Molecules 4 Expert Committee intends to revise the Chlorpromazine Hydrochloride Tablets monograph.

Based on the supporting data received from a manufacturer awaiting FDA approval, the Expert Committee proposes to revise the Chlorpromazine Hydrochloride Tablets monograph to add *Dissolution Test 3*.

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.[1]

Should you have any questions, please contact Yanyin Yang, Senior Scientist II (301-692-3623 or yanyin.yang@usp.org).

[1] 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*.

Notice of Intent to Revise
Official: To Be Determined

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

● **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 ethyl ether 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 ($C_{17}H_{19}ClN_2S \cdot HCl$) 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* (µg/mL)

C_U = nominal concentration of chlorpromazine hydrochloride in the *Sample solution* (µg/mL)

Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS

Change to read:

- **Dissolution** ⟨711⟩

Test 1

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 ($C_{17}H_{19}ClN_2S \cdot HCl$) dissolved.

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

▲**Test 3:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

Medium: 0.1 N hydrochloric acid; 500 mL

Apparatus 1: 100 rpm

Time: 30 min

Standard stock solution: 0.6 mg/mL of USP Chlorpromazine Hydrochloride RS in acetonitrile. Sonicate to dissolve, if necessary.

Standard solution: 0.006 mg/mL of USP Chlorpromazine Hydrochloride RS from the *Standard stock solution* in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding an appropriate volume of filtrate so that a consistent result can be obtained. Dilute with *Medium* to a concentration similar to that of the *Standard solution*.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV-Vis

Analytical wavelength: UV 254 nm

Blank: *Medium*

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* (mg/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 ▲ (TBD)

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

IMPURITIES

- **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 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.
- **Labeling:** The labeling states the *Dissolution* test used only if *Test 1* is not used.
- **USP Reference Standards** ⟨11⟩

USP Chlorpromazine Hydrochloride RS

Page Information:

Not Applicable

Current DocID: