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Chlorpromazine Hydrochloride Oral Concentrate

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click https://www.uspnf.com/rb-chlorpromazine-hcl-oral-conc-20210614.

DEFINITION

Chlorpromazine Hydrochloride Oral Concentrate contains NLT 90.0% and NMT 110.0% 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 analyses without delay, under subdued light, or using low-actinic glassware.]

IDENTIFICATION

Change to read:

• **A.**

Standard solution: 0.2 mg/mL of USP Chlorpromazine Hydrochloride RS in methanol

Sample solution: Transfer a portion of Oral Concentration, equivalent to 20 mg of chlorpromazine hydrochloride, to a 125-mL separator. Add 10 mL of water and 2 mL of sodium hydroxide solution (1 in 2). Extract with three 30-mL portions of ▲ethyl ether.▲ (RB 15-Jun-2021) Filter the combined ▲ethyl ether▲ (RB 15-Jun-2021) extracts through anhydrous sodium sulfate. With the aid of a stream of nitrogen evaporate the ▲ethyl ether▲ (RB 15-Jun-2021) to about 5 mL. Quantitatively transfer the solution to a 40-mL centrifuge tube. Evaporate with a stream of nitrogen and mild heat to dryness. Dissolve the residue in 100 mL of methanol.

Chromatographic system

(See *Chromatography ⟨621⟩, General Procedures, Thin-Layer Chromatography*.)

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel

Spray reagent: Dissolve 100 mg of platinic chloride in 10 mL of 0.1 N hydrochloric acid, add 25 mL of potassium iodide solution (1 in 25), 0.5 mL of formic acid, and dilute with water to 100 mL.

Application volume: 15 µL

Developing solvent system: Freshly prepared mixture of ethyl acetate that has been saturated with ammonium hydroxide, ▲ethyl ether,▲ (RB 15-Jun-2021) and methanol (75:25:20)

Analysis

Samples: *Standard solution* and *Sample solution*

Develop the chromatogram in the *Developing solvent system* until the solvent front has moved three-fourths of the length of the plate. Remove the plate from the chamber, air-dry, and spray with *Spray reagent*.

Acceptance criteria: The R_F value of the principal spot of the *Sample solution* corresponds to that of the *Standard solution*.

• **B.** Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Chloride*

Sample solution: Dilute a portion of the Oral Concentrate with an equal volume of water.

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 from Oral Concentrate prepared as follows. Transfer a portion of Oral Concentrate, previously diluted if necessary, equivalent to about 10 mg of chlorpromazine hydrochloride, to a 50-mL volumetric flask. Dilute with 0.1 N hydrochloric acid to volume.

Sample solution: Nominally 8 µg/mL of chlorpromazine hydrochloride from *Sample stock solution* prepared as follows. Pipet 10 mL of the *Sample stock solution* into a 250-mL separator, add about 20 mL of water, render alkaline with ammonium hydroxide, and extract with four 25-mL portions of ▲ethyl ether.▲ (RB 15-Jun-2021) Extract the combined ▲ethyl ether▲ (RB 15-Jun-2021) 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 15-Jun-2021) and add 0.1 N hydrochloric acid to volume.

Instrumental conditions

Mode: UV-Vis

Analytical wavelengths: Maximum absorbance at about 254 and 277 nm

Cell: 1 cm

Blank: 0.1 N hydrochloric acid

Analysis: Calculate the percentage of the labeled amount of chlorpromazine hydrochloride ($C_{17}H_{19}ClN_2S \cdot HCl$) in the portion of Oral Concentrate 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: 90.0%–110.0%

IMPURITIES

Change to read:

• **Limit of Chlorpromazine Sulfoxide**

Chlorpromazine sulfoxide standard stock solution 1: 10.6 mg/mL of USP Chlorpromazine Hydrochloride RS in dilute hydrochloric acid (1 in 100)

Chlorpromazine sulfoxide standard stock solution 2: Transfer 5 mL of *Chlorpromazine sulfoxide standard stock solution 1* to a 50-mL volumetric flask. Add 2 mL of 30% hydrogen peroxide and heat at 60° for 10 min. Cool, and dilute with 1 M sodium bisulfite to volume.

Chlorpromazine sulfoxide standard solution: 1 mg/mL of chlopromazine sulfoxide prepared as follows. Transfer 10.0 mL of *Chlorpromazine sulfoxide standard stock solution 2* to a 60-mL separator, and add 2 mL of sodium hydroxide solution (1 in 2). Extract with three 30-mL portions of ▲ethyl ether.▲ (RB 15-Jun-2021) Filter the extracts through ▲ethyl ether▲ (RB 15-Jun-2021) -wetted anhydrous sodium sulfate into a 250-mL conical flask. Cautiously evaporate the extracts to dryness. Dissolve the residue in 10.0 mL of methanol, and filter if necessary.

Sample solution: Transfer a portion of Oral Concentration, equivalent of 20 mg of chlorpromazine hydrochloride, to a 125-mL separator. Add 10 mL of water and 2 mL of sodium hydroxide solution (1 in 2). Extract with three 30-mL portions of ▲ethyl ether.▲ (RB 15-Jun-2021) Filter the combined ▲ethyl ether▲ (RB 15-Jun-2021) extracts through anhydrous sodium sulfate. With the aid of a stream of nitrogen evaporate the ▲ethyl ether▲ (RB 15-Jun-2021) to about 5 mL. Quantitatively transfer the solution to a 40-mL centrifuge tube. Evaporate with a stream of nitrogen and mild heat to dryness. Dissolve the residue in 1.0 mL of methanol.

Chromatographic system

(See *Chromatography ⟨621⟩, Procedures, Thin-Layer Chromatography*.)

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel

Spray reagent: Dissolve 100 mg of platinic chloride in 10 mL of 0.1 N hydrochloric acid, add 25 mL of potassium iodide solution (1 in 25), 0.5 mL of formic acid, and dilute with water to 100 mL.

Application volume: 15 µL

Developing solvent system: Freshly prepared mixture of ethyl acetate that has been saturated with ammonium hydroxide, ▲ethyl ether,▲ (RB 15-Jun-2021) and methanol (75:25:20)

Analysis

Samples: *Chlorpromazine sulfoxide standard solution* and *Sample solution*

Develop the chromatogram in the *Developing solvent system* until the solvent front has moved three-fourths of the length of the plate. Remove the plate from the chamber, air-dry, and spray with *Spray reagent*.

Acceptance criteria: The chromatogram from the *Sample solution* may exhibit a secondary spot whose R_F value corresponds to, and whose size and intensity are not greater than, those of the spot of the *Chlorpromazine sulfoxide standard solution* (5.0%).

SPECIFIC TESTS

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** It meets the requirements for the absence of *Escherichia coli*.

Change to read:

• **pH ⟨791⟩:** 2.3–▲5.0▲ (RB 15-Jun-2021)

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers.

• **Labeling:** Label it to indicate that it must be diluted prior to administration.

• **USP Reference Standards ⟨11⟩**
USP Chlorpromazine Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
CHLORPROMAZINE HYDROCHLORIDE ORAL CONCENTRATE	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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