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Chlorpromazine Hydrochloride Oral Concentrate

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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 \(521\)](#), [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 chlorpromazine 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