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Chlorpheniramine Maleate and Pseudoephedrine Hydrochloride Extended-Release Capsules

» Chlorpheniramine Maleate and Pseudoephedrine Hydrochloride Extended-Release Capsules contain not less than 90.0 percent and not more than 110.0 percent of the labeled amounts of chlorpheniramine maleate ($C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$) and pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$).

Packaging and storage—Preserve in tight, light-resistant containers, and store at controlled room temperature.

Labeling—The labeling indicates the *Dissolution Test* with which the product complies.

USP Reference standards ⟨11⟩—
USP Chlorpheniramine Maleate RS
USP Pseudoephedrine Hydrochloride RS

Identification—

A: The retention time of the major peak for chlorpheniramine maleate in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay for chlorpheniramine maleate.*

B: The retention time of the major peak for pseudoephedrine hydrochloride in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay for pseudoephedrine hydrochloride.*

Dissolution ⟨711⟩—

TEST 1—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 1.*

Medium: water; 900 mL.

Apparatus 2: 50 rpm.

Times: 3, 6, and 12 hours.

Procedure—Determine the amounts of chlorpheniramine maleate ($C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$) and pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) dissolved by employing the methods set forth in the *Assay for chlorpheniramine maleate* and the *Assay for pseudoephedrine hydrochloride*, respectively.

Tolerances—The percentages of the labeled amounts of $C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$ and $C_{10}H_{15}NO \cdot HCl$ dissolved at the specified times conform to *Acceptance Table 2.*

Time (hours)	Amount dissolved
3	between 20% and 50%
6	between 45% and 75%
12	not less than 75%

TEST 2—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2.*

Medium 1: simulated gastric fluid TS, prepared without pepsin; 900 mL.

Medium 2: simulated intestinal fluid TS, prepared without pancreatin; 900 mL.

Apparatus 2: 50 rpm.

Time for Medium 1: 1.5 hours.

Times for Medium 2: 3 and 6 hours.

Procedure—Determine the amounts of chlorpheniramine maleate ($C_{16}N_{19}ClN_2 \cdot C_4H_4O_4$) and pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) dissolved by employing the methods set forth in the *Assay for chlorpheniramine maleate* and the *Assay for pseudoephedrine*

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hydrochloride, respectively, using Standard solutions having known concentrations of the relevant USP Reference Standard in the appropriate *Medium*.

Tolerances—The percentages of the labeled amounts of $C_{16}N_{19}ClN_2 \cdot C_4H_4O_4$ and $C_{10}H_{15}NO \cdot HCl$ dissolved at the specified times conform to *Acceptance Table 2*.

Time (hours)	Amount dissolved (*Medium 1*)	Amount dissolved (*Medium 2*)
1.5	between 15% and 40%	
3.0		between 35% and 75%
6.0		not less than 50%

Uniformity of dosage units ⟨905⟩: meet the requirements.

Assay for chlorpheniramine maleate—

Mobile phase—Prepare a filtered and degassed mixture of methanol and water (60:40) containing 0.34 g of monobasic potassium phosphate, 0.15 g of triethylamine hydrochloride, 0.25 g of sodium lauryl sulfate, and 0.1 mL of phosphoric acid in each 100 mL of solution. Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Standard preparation—Dissolve an accurately weighed quantity of USP Chlorpheniramine Maleate RS in water to obtain a solution having a known concentration of about 0.8 mg per mL. Quantitatively dilute a portion of this solution with a phosphoric acid solution (1 in 1000) to obtain a solution having a known concentration of about 8 µg per mL.

Assay preparation—Transfer not fewer than 10 Capsules to a suitable container. Add 100 mL of water and 10 mL of a phosphoric acid solution (1 in 20), and heat gently until the Capsules are fully dispersed. Cool to room temperature, and transfer an accurately measured volume of the solution, equivalent to about 0.8 mg of chlorpheniramine maleate, to a 100-mL volumetric flask. Dilute with water to volume, mix, and filter.

System suitability solution—Mix 1 part of the *Standard preparation* prepared above with 1 part of the *Standard preparation,* prepared as directed in the *Assay for pseudoephedrine hydrochloride*.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 214-nm detector and a 4.6-mm × 15-cm column that contains packing L11. The flow rate is about 2 mL per minute. Inject about 20 µL of the *System suitability solution*, and record the peak responses as directed for *Procedure:* the resolution, *R,* between pseudoephedrine and chlorpheniramine is not less than 2.0. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the tailing factor for the chlorpheniramine peak is not greater than 2.0; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the chlorpheniramine peaks. Calculate the quantity, in mg, of chlorpheniramine maleate ($C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$) in the portion of Capsules taken by the formula:

$$100C(r_U/r_S)$$

in which C is the concentration, in µg per mL, of USP Chlorpheniramine Maleate RS in the *Standard preparation;* and r_U and r_S are the chlorpheniramine peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Assay for pseudoephedrine hydrochloride—

Mobile phase and *Chromatographic system*—Proceed as directed in the *Assay for chlorpheniramine maleate*.

Standard preparation—Dissolve an accurately weighed quantity of USP Pseudoephedrine Hydrochloride RS in water to obtain a solution having a known concentration of about 3.0 mg per mL. Transfer about 1.0 mL of this solution to a 25-mL volumetric flask, dilute with 0.1% phosphoric acid to volume, and mix.

System suitability solution—Mix 1 part of the *Standard preparation* prepared above with 1 part of the *Standard preparation* prepared as directed in the *Assay for chlorpheniramine maleate*.

Assay preparation—Transfer not fewer than 10 Capsules to a suitable container. Add 100 mL of water and 10 mL of a phosphoric acid solution (1 in 20), and heat gently until the Capsules are fully dispersed. Cool to room temperature, and transfer an accurately measured volume of the solution, equivalent to about 12 mg of pseudoephedrine hydrochloride, to a 100-mL volumetric flask. Dilute with water to volume, mix, and filter.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the pseudoephedrine peaks. Calculate the quantity, in mg, of pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) in the portion of Capsules taken by the formula:

$$100C(r_U/r_S)$$

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