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Chlorpheniramine Maleate Extended-Release Capsules

» Chlorpheniramine Maleate Extended-Release Capsules contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of chlorpheniramine maleate ($C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$).

Packaging and storage—Preserve in tight containers.

Labeling—Label the Capsules to indicate the *Dissolution Test* with which the product complies.

USP Reference standards ⟨11⟩—
USP Chlorpheniramine Maleate RS

Identification—

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

B: Transfer the contents of 1 Capsule to a 10-mL volumetric flask, add 5 mL of methanol, and insert the stopper into the flask. Sonicate this solution for 10 minutes, dilute with water to volume, mix, and filter. Apply separately 10 µL of this solution and 10 µL of a solution of USP Chlorpheniramine Maleate RS in a mixture of methanol and water (1:1) containing about 1.2 mg per mL to a suitable thin-layer chromatographic plate (see *Chromatography* ⟨621⟩) coated with a 0.25-mm layer of chromatographic silica gel mixture. Allow the spots to dry, and develop the chromatogram in a solvent system consisting of a mixture of ethyl acetate, methanol, and ammonium hydroxide (100:5:5) until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the chamber, mark the solvent front, allow the solvent to evaporate, and examine the plate under short-wavelength UV light: the R_F value of the principal spot observed in the chromatogram of the solution under test corresponds to that obtained from the Standard solution.

Dissolution ⟨711⟩—

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

Medium: water; 500 mL.

Apparatus 1: 100 rpm.

Times: 1.5, 6.0, and 10.0 hours.

Procedure—Determine the amount of $C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$ dissolved by employing the method set forth in the *Assay*, using a filtered portion of the solution under test in comparison with a Standard solution having a known concentration of USP Chlorpheniramine Maleate RS in the same medium.

Tolerances—The percentages of the labeled amount of $C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$ dissolved at the times specified conform to *Acceptance Table 2*.

Time (hours)	Amount dissolved
1.5	between 15% and 40%
6.0	between 50% and 80%
10.0	not less than 70%

TEST 2—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2.* Proceed as directed for *Procedure* for *Method B* under *Apparatus 1 and Apparatus 2, Delayed-Release Dosage Forms.*

Medium—Prepare as directed under *Method B,* except use 900 mL of media. Operate the apparatus for 1 hour in the *Acid Stage* and use the acceptance criteria given under *Tolerances*. Operate the apparatus for 6 hours in the *Buffer Stage*, except to use 900 mL of simulated intestinal fluid TS without enzyme, and use the acceptance criteria given under *Tolerances*.

Apparatus 2: 50 rpm.

Times: 1.0 hour, 3.0 hours, 7.0 hours.

Procedure—Proceed as directed in *Test 1*.

Tolerances—The percentages of the labeled amount of $C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$ dissolved at the times specified conform to *Acceptance Table 2.*

Time (hours)	Amount dissolved
1.0	between 30% and 60%
3.0	between 55% and 85%
7.0	not less than 70%

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

Assay—

Mobile phase—Dissolve 2.0 g of sodium perchlorate in 350 mL of water. Add 650 mL of methanol and 2.0 mL of triethylamine, and mix. Filter, and degas this solution prior to use. Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Standard preparation—Dissolve an accurately weighed quantity of USP Chlorpheniramine Maleate RS in dilute hydrochloric acid (1 in 100) to obtain a solution having a known concentration of about 0.12 mg per mL.

Assay preparation—Weigh and mix the contents of not fewer than 20 Capsules. Transfer an accurately weighed portion of the mixture, equivalent to about 120 mg of chlorpheniramine maleate, to a 200-mL volumetric flask. Add about 100 mL of dilute hydrochloric acid (1 in 100), bring to a boil on a hot plate, and continue boiling moderately for 5 minutes. Cool, dilute with dilute hydrochloric acid (1 in 100) to volume, mix, and filter. Transfer 10.0 mL of the filtrate to a 50-mL volumetric flask, dilute with dilute hydrochloric acid (1 in 100) to volume, and mix.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 261-nm detector and a 3.9-mm × 15-cm column that contains 10-µm packing L1. The flow rate is about 1 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the column efficiency is not less than 900 theoretical plates, the tailing factor is not greater than 2.0, and the relative standard deviation for replicate injections is not more than 1.5%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major 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:

$$(1000C)(r_U/r_S)$$

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

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

Topic/Question	Contact	Expert Committee
CHLORPHENIRAMINE MALEATE EXTENDED-RELEASE CAPSULES	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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