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Oral Solution Containing at Least Three of the Following—Acetaminophen and Salts of Chlorpheniramine, Dextromethorphan, and Pseudoephedrine

» Oral Solution Containing at Least Three of the Following—Acetaminophen and Salts of Chlorpheniramine, Dextromethorphan, and Pseudoephedrine contains not less than 90.0 percent and not more than 110.0 percent of the labeled amounts of acetaminophen ($C_8H_9NO_2$), chlorpheniramine maleate ($C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$), dextromethorphan hydrobromide ($C_{18}H_{25}NO \cdot HBr \cdot H_2O$), and pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) or pseudoephedrine sulfate [$(C_{10}H_{15}NO)_2 \cdot H_2SO_4$].

[Note—The heading of this monograph does not constitute the official title. It is not intended that the name described herein be recognized as the official title or the common or usual name. The name for each article encompassed by this monograph shall be composed of the names of the active ingredients contained therein, as well as the quantitative amount of each active ingredient, and a statement of the function (or purpose) of the ingredient in the article.]

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

USP Reference standards ⟨11⟩—

USP Acetaminophen RS
USP Chlorpheniramine Maleate RS
USP Dextromethorphan Hydrobromide RS
USP Pseudoephedrine Hydrochloride RS
USP Pseudoephedrine Sulfate RS

Labeling—The label for each article encompassed by this monograph bears a name composed of the active ingredients. The label states the name and quantity of each active ingredient and indicates its function (or purpose) in the article.

Identification—

A: If pseudoephedrine hydrochloride or pseudoephedrine sulfate is claimed in the labeling to be present, the retention time of the major peak for pseudoephedrine 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* or the *Assay for pseudoephedrine sulfate.*

B: If acetaminophen is claimed in the labeling to be present, the retention time of the major peak for acetaminophen in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay for acetaminophen.*

C: If chlorpheniramine maleate is claimed in the labeling to be present, the retention time of the major peak for chlorpheniramine 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.*

D: If dextromethorphan hydrobromide is claimed in the labeling to be present, the retention time of the major peak for *dextromethorphan* in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay for dextromethorphan hydrobromide.*

Uniformity of dosage units ⟨905⟩—

FOR ORAL SOLUTION PACKAGED IN SINGLE-UNIT CONTAINERS: meets the requirements.

Deliverable volume ⟨698⟩—

FOR ORAL SOLUTION PACKAGED IN MULTIPLE-UNIT CONTAINERS:meets the requirements.

pH ⟨791⟩**:** between 3.7 and 7.5.

Alcohol Determination, *Method II* ⟨611⟩*(if present)* **:** between 90.0% and 110.0% of the labeled amount of C_2H_5OH.

Microbial enumeration tests ⟨61⟩ **and Absence of specified microorganisms** ⟨62⟩—The total bacterial count does not exceed 100 cfu per g, the total combined molds and yeasts count does not exceed 10 cfu per g, and it meets the requirements of the tests for absence of *Salmonella* species and *Escherichia coli.*

Assay for pseudoephedrine hydrochloride (where pseudoephedrine hydrochloride is the salt form used, if present in the formulation)—

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 Pseudoephedrine Hydrochloride RS in water to obtain a solution having a known concentration of about 1.5 mg per mL. Transfer 1.0 mL of this solution to a 10-mL volumetric flask, add 8.0 mL of *Mobile phase,* dilute with water to volume, and mix.

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Chlorpheniramine standard preparation—Prepare as directed for *Standard preparation* in the *Assay for chlorpheniramine maleate.*

Dextromethorphan standard preparation—Prepare as directed for *Standard preparation* in the *Assay for dextromethorphan hydrobromide.*

System suitability solution 1 (for Oral Solution that contains either all the four ingredients or a combination of three containing chlorpheniramine salt)—Mix equal volumes of the *Standard preparation* and the *Chlorpheniramine standard preparation.*

System suitability solution 2 (for Oral Solution that contains no chlorpheniramine salt)—Mix equal volumes of the *Standard preparation* and the *Dextromethorphan standard preparation.*

Assay preparation—Transfer an accurately measured volume of the Oral Solution, equivalent to 15 mg of pseudoephedrine hydrochloride, to a 100-mL volumetric flask, add 80.0 mL of *Mobile phase*, dilute with water to volume, and mix.

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. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the tailing factor for the pseudoephedrine peak is not greater than 2.5; and the relative standard deviation for replicate injections is not more than 2.0%. Separately inject about 10 µL of *System suitability solution 1* or *System suitability solution 2,* as appropriate. The resolution, *R,* between pseudoephedrine and chlorpheniramine or between pseudoephedrine and dextromethorphan is not less 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 pseudoephedrine peaks. Calculate the quantity, in mg, of pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) in each mL of the Oral Solution taken by the formula:

$$100(C/V)(r_U/r_S)$$

in which C is the concentration, in mg per mL, of USP Pseudoephedrine Hydrochloride RS in the *Standard preparation; V* is the volume, in mL, of the Oral Solution taken; and r_U and r_S are the pseudoephedrine peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Assay for pseudoephedrine sulfate (where pseudoephedrine sulfate is the salt form used, if present in the formulation)—

Mobile phase, System suitability solutions, and *Chromatographic system*—Proceed as directed in the *Assay for pseudoephedrine hydrochloride.*

Chlorpheniramine standard preparation—Prepare as directed for *Standard preparation* in the *Assay for chlorpheniramine maleate.*

Dextromethorphan standard preparation—Prepare as directed for *Standard preparation* in the *Assay for dextromethorphan hydrobromide.*

Standard preparation—Dissolve an accurately weighed quantity of USP Pseudoephedrine Sulfate RS in water to obtain a solution having a known concentration of about 3.0 mg per mL. Transfer 1.0 mL of this solution to a 10-mL volumetric flask, add 4.0 mL of *Mobile phase,* dilute with water to volume, and mix.

Assay preparation—Transfer an accurately measured volume of Oral Solution, equivalent to 30 mg of pseudoephedrine sulfate, to a 100-mL volumetric flask, add 80.0 mL of *Mobile phase,* dilute with water to volume, and mix.

Procedure—Proceed as directed for *Procedure* in the *Assay for pseudoephedrine hydrochloride.* Calculate the quantity, in mg, of pseudoephedrine sulfate [$(C_{10}H_{15}NO)_2 \cdot H_2SO_4$] in each mL of the Oral Solution taken by the formula:

$$100(C/V)(r_U/r_S)$$

in which the terms are as defined therein, pseudoephedrine sulfate being substituted for pseudoephedrine hydrochloride.

Assay for acetaminophen *(if present)*—

Mobile phase—Prepare a suitable degassed and filtered mixture of water, methanol, and glacial acetic acid (79:20:1). Make any necessary adjustments (see *System Suitability* under *Chromatography ⟨621⟩*).

Standard preparation—Transfer about 16.5 mg of USP Acetaminophen RS, accurately weighed, to a 100-mL volumetric flask. Add 2.5 mL of methanol, and mix until solution is complete. Dilute with water to volume, and mix to obtain a solution having a known concentration of about 0.165 mg per mL.

Assay preparation—Transfer an accurately measured volume of Oral Solution, equivalent to about 33 mg of acetaminophen, to a 200-mL volumetric flask, add 5 mL of methanol, and mix. Dilute with water to volume, and mix.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 280-nm detector and a 4.6-mm × 15-cm column that contains packing L7. The flow rate is about 1 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the tailing factor for the acetaminophen 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 acetaminophen peaks. Calculate the quantity, in mg, of acetaminophen ($C_8H_9NO_2$) in each mL of the Oral Solution taken by the formula:

$$200(C/V)(r_U/r_S)$$

in which C is the concentration, in mg per mL, of USP Acetaminophen RS in the *Standard preparation; V* is the volume, in mL, of the Oral Solution taken; and r_U and r_S are the acetaminophen peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Assay for chlorpheniramine maleate *(if present)*—

Mobile phase and *Chromatographic system*—Proceed as directed in the *Assay for pseudoephedrine hydrochloride.*

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