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Guaifenesin, Pseudoephedrine Hydrochloride, and Dextromethorphan Hydrobromide Capsules

» Guaifenesin, Pseudoephedrine Hydrochloride, and Dextromethorphan Hydrobromide Capsules contain not less than 90.0 percent and not more than 110.0 percent of the labeled amounts of guaifenesin ($C_{10}H_{14}O_4$), pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$), and dextromethorphan hydrobromide ($C_{18}H_{25}NO \cdot HBr \cdot H_2O$).

Packaging and storage—Preserve in tight, light-resistant containers.

USP Reference standards ⟨11⟩—
USP Dextromethorphan Hydrobromide RS
USP Guaifenesin RS
USP Pseudoephedrine Hydrochloride RS

Identification—

A: The retention time of the guaifenesin peak relative to that of the benzoic acid peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation* as obtained in the *Assay for guaifenesin*.

B: The retention times of the pseudoephedrine and dextromethorphan peaks in the chromatogram of the *Assay preparation* relative to that of the brompheniramine peak correspond to those in the chromatogram of the *Standard preparation* as obtained in the *Assay for pseudoephedrine hydrochloride and dextromethorphan hydrobromide*.

Uniformity of dosage units ⟨905⟩—

Procedure for content uniformity of pseudoephedrine hydrochloride and *dextromethorphan hydrobromide*—Proceed as directed in the *Assay for pseudoephedrine hydrochloride and dextromethorphan hydrobromide*, preparing the *Assay preparation* as follows. Transfer 1 Capsule to a 100-mL volumetric flask, add about 50 mL of water, heat on a steam bath for about 15 minutes, and allow to cool. Add 5.0 mL of *Internal standard solution*, dilute with water to volume, and mix.

Assay for guaifenesin—

Mobile phase, Internal standard solution, Standard stock solution, Standard preparation, and *Chromatographic system*—Proceed as directed in the *Assay for guaifenesin* under *Guaifenesin and Pseudoephedrine Hydrochloride Capsules*.

Assay preparation—Transfer an accurately counted number of Capsules, equivalent to about 2000 mg of guaifenesin, to a 100-mL volumetric flask, add about 50 mL of water, and heat on a steam bath for about 15 minutes. Allow to cool, dilute with water to volume, and mix (stock solution). Transfer 10.0 mL of this stock solution to a second 100-mL volumetric flask, dilute with water to volume, and mix. Transfer 5.0 mL of this solution and 5.0 mL of *Internal standard solution* to a third 100-mL volumetric flask, add about 40 mL of methanol, dilute with water to volume, and mix.

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 area responses for the major peaks. Calculate the quantity, in mg, of guaifenesin ($C_{10}H_{14}O_4$) in each Capsule taken by the formula:

$$20{,}000(C/N)(R_U/R_S)$$

in which C is the concentration, in mg per mL, of USP Guaifenesin RS in the *Standard preparation*, N is the number of Capsules taken, and R_U and R_S are the ratios of the guaifenesin peak area response to the benzoic acid peak area response obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Assay for pseudoephedrine hydrochloride and dextromethorphan hydrobromide—

Mobile phase—To 3.5 g of docusate sodium add 500 mL of methanol, 350 mL of water, 145 mL of tetrahydrofuran, and 5 mL of glacial acetic acid, mix, and pass through a filter having a porosity of 0.5 µm or less. Make any necessary adjustments (see *System Suitability* under *Chromatography ⟨621⟩*).

Internal standard solution—Prepare a solution of brompheniramine maleate in methanol containing about 0.3 mg per mL.

Standard stock solution—Prepare a solution in water having known concentrations of about 20 mg of USP Guaifenesin RS, 20*J* mg of USP Pseudoephedrine Hydrochloride RS per mL, and 20*J'* mg of USP Dextromethorphan Hydrobromide RS per mL, *J* being the ratio of the labeled amount, in mg, of pseudoephedrine hydrochloride to the labeled amount, in mg, of guaifenesin per Capsule, and *J'* being the ratio of the labeled amount, in mg, of dextromethorphan hydrobromide to the labeled amount, in mg, of guaifenesin per Capsule.

Standard preparation—Transfer 10.0 mL of *Standard stock solution* and 5.0 mL of *Internal standard solution* to a 100-mL volumetric flask, dilute with water to volume, and mix.

Assay preparation—Transfer 10.0 mL of the stock solution used to prepare the *Assay preparation* in the *Assay for guaifenesin* and 5.0 mL of *Internal standard solution* to a 100-mL volumetric flask, dilute with water to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 263-nm detector and a 3.9-mm × 30-cm column that contains packing L1. The flow rate is about 2 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed under *Procedure:* the relative retention times are about 0.4 for pseudoephedrine, 0.75 for dextromethorphan, and 1.0 for brompheniramine; the resolution, *R,* between the peaks is not less than 1.5; the tailing factors for the pseudoephedrine peak, the dextromethorphan peak, and the brompheniramine peak are not more than 1.5, 2.5, and 3.0, respectively; and the relative standard deviation for replicate injections determined for the pseudoephedrine peak is not more than 2.0%.

Procedure—Separately inject equal volumes (about 50 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the area responses for the major peaks. Calculate the quantity, in mg, of pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) in each Capsule taken by the formula:

$$1000(C/N)(R_U/R_S)$$

in which *C* is the concentration, in mg per mL, of USP Pseudoephedrine Hydrochloride RS in the *Standard preparation; N* is the number of Capsules taken; and R_U and R_S are the ratios of the pseudoephedrine peak area response to the brompheniramine peak area response obtained from the *Assay preparation* and the *Standard preparation,* respectively. Calculate the quantity, in mg, of dextromethorphan hydrobromide ($C_{18}H_{25}NO \cdot HBr \cdot H_2O$) in each Capsule taken by the formula:

$$1000(370.33/352.31)(C/N)(R_U/R_S)$$

in which 370.33 and 352.31 are the molecular weights of dextromethorphan hydrobromide and anhydrous dextromethorphan hydrobromide, respectively; *C* is the concentration, in mg per mL, of USP Dextromethorphan Hydrobromide RS in the *Standard preparation; N* is the number of Capsules taken; and R_U and R_S are the ratios of the dextromethorphan peak area response to the brompheniramine peak response 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
GUAIFENESIN, PSEUDOEPHEDRINE HYDROCHLORIDE, AND DEXTROMETHORPHAN HYDROBROMIDE CAPSULES	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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