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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 μ L) 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 μ m 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](#), 20J mg of [USP Pseudoephedrine Hydrochloride RS](#) per mL, and 20J' 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 (C₁₀H₁₅NO · HCl) in each Capsule taken by the formula:

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

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_J* 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 (C₁₈H₂₅NO · HBr · H₂O) in each Capsule taken by the formula:

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

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_J* 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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