Risk Levels, High-Risk Level CSPs apply. After successful completion of sterility testing, the *Beyond-Use Date* is NMT 60 days after the date on which it was compounded when stored at controlled room temperature.

- **LABELING:** Label it to state the *Beyond-Use Date*. The label indicates that the Solution is not to be used if it contains a precipitate. Label it to state that it is a single-unit container, that it is overfilled with an excess that should be discarded after a measured single dose is used, and to store at controlled room temperature. Label it for inhalation or oral administration only. Label it to state that the preparation may have a disagreeable odor and light purple color that is a result of a chemical reaction that does not affect the strength of the preparation.
- **USP REFERENCE STANDARDS** ⟨11⟩
USP Acetylcysteine RS

Acetylcysteine and Isoproterenol Hydrochloride Inhalation Solution

» Acetylcysteine and Isoproterenol Hydrochloride Inhalation Solution is a sterile solution of Acetylcysteine and Isoproterenol Hydrochloride in water. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of acetylcysteine ($C_5H_9NO_3S$), and not less than 90.0 percent and not more than 115.0 percent of the labeled amount of isoproterenol hydrochloride ($C_{11}H_{17}NO_3 \cdot HCl$).

Packaging and storage—Preserve in single-dose or multiple-dose containers, preferably of Type I glass, tightly closed with a glass or polyethylene closure, and store at controlled room temperature.

Labeling—The label indicates that the Inhalation Solution is not to be used if its color is pinkish or darker than slightly yellow or if it contains a precipitate.

USP Reference standards ⟨11⟩—
USP Acetylcysteine RS
USP Isoproterenol Hydrochloride RS
USP L-Phenylalanine RS

Color and clarity—Using the Inhalation Solution as the *Test solution*, proceed as directed for *Color and clarity* under *Isoproterenol Inhalation Solution*.

Identification—

A: Place 2 mL in a 10-mL beaker, and adjust with 3 N hydrochloric acid to a pH of about 3 (pH indicator paper). Add 500 mg to 1 g of finely powdered sodium chloride, in two portions of about 200 mg each initially, and then in smaller portions (about 25 mg), stirring after each addition, until a precipitate is formed. Allow to stand at room temperature for 15 minutes, and collect the residue by suction filtration: the acetylcysteine so obtained, after being dried as directed in the test for *Loss on drying* under *Acetylcysteine*, responds to the *Identification* test under *Acetylcysteine*.

B: *Ferro-Citrate Solution* and *Buffer Solution*—Prepare as directed under *Epinephrine Assay* ⟨391⟩.

Procedure—Place a volume of Inhalation Solution, equivalent to about 0.26 mg of isoproterenol hydrochloride, in a test tube with 3 mL of 0.1 M mercuric chloride, and mix. Add 100 µL of *Ferro-Citrate Solution* and 1.0 mL of *Buffer Solution*, and mix: the presence of isoproterenol hydrochloride is confirmed by the development of a purple color.

Sterility Tests ⟨71⟩: meets the requirements.

pH ⟨791⟩: between 6.0 and 7.0.

Assay for acetylcysteine—

Mobile phase, Internal standard solution, Standard preparation, and *Chromatographic system*—Proceed as directed in the *Assay* under *Acetylcysteine*.

Assay preparation—Pipet a volume of Inhalation Solution, equivalent to about 1000 mg of acetylcysteine, into a 100-mL volumetric flask, dilute with sodium metabisulfite solution (1 in 2000) to volume, and mix. Pipet 10 mL of this solution and 10 mL of *Internal standard solution* into a 200-mL volumetric flask, dilute with sodium metabisulfite solution (1 in 2000) to volume, and mix.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Acetylcysteine*. Calculate the quantity, in mg, of $C_5H_9NO_3S$ in each mL of the Inhalation Solution taken by the formula:

$$2000(C/V)(R_U / R_S)$$

in which C is the concentration, in mg per mL, of USP Acetylcysteine RS in the *Standard preparation; V* is the volume, in mL, of Inhalation Solution taken; and R_U and R_S are the ratios of the peak response of acetylcysteine to that of DL-phenylalanine obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Assay for isoproterenol hydrochloride—

Mobile phase—Dissolve 13.6 g of monobasic potassium phosphate in 1000 mL of water, and pass through a membrane filter having a 0.45-µm porosity. Add 20.0 mL of methanol, mix, and degas.

Internal standard solution—Place about 150 mg of acetaminophen in a 500-mL volumetric flask, add 5 mL of glacial acetic acid, dilute with water to volume, and mix.

Standard preparation—Dissolve an accurately weighed quantity of USP Isoproterenol Hydrochloride RS in 0.05 M sodium metabisulfite to obtain a solution having a known concentration of 0.15 mg per mL. Transfer 10.0 mL of this solution to a 25-mL volumetric flask, add 10.0 mL of *Internal standard solution,* dilute with 0.2 M acetic acid to volume, and mix.

Assay preparation—Transfer an accurately measured volume of Inhalation Solution, equivalent to about 1.5 mg of isoproterenol hydrochloride, and 10 mL of *Internal standard solution* to a 25-mL volumetric flask, add dilute glacial acetic acid (1 in 100) to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 280-nm detector and a 3.9-mm × 40-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 for *Procedure:* the relative retention times are about 0.5 for isoproterenol hydrochloride and 1.0 for acetaminophen; the resolution, *R,* between isoproterenol hydrochloride and acetaminophen is not less than 6; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 25 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 isoproterenol hydrochloride ($C_{11}H_{17}NO_3 \cdot HCl$) in each mL of the Inhalation Solution taken by the formula:

$$(25C/V)(R_U / R_S)$$

in which C is the concentration, in mg per mL, of USP Isoproterenol Hydrochloride RS in the *Standard preparation; V* is the volume, in mL, of Inhalation Solution taken; and R_U and R_S are the ratios of the peak responses of isoproterenol hydrochloride to those of acetaminophen obtained from the *Assay preparation* and the *Standard preparation,* respectively.