» Isoetharine Mesylate contains not less than 97.0 percent and not more than 102.0 percent of $C_{13}H_{21}NO_3 \cdot CH_4O_3S$, calculated on the dried basis.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—
USP Isoetharine Hydrochloride RS

Identification—

A: It responds to the *Thin-layer Chromatographic Identification Test* ⟨201⟩, the test solution and the Standard solution of USP Isoetharine Hydrochloride RS being prepared at a concentration of 2.5 mg per mL in methanol, the solvent mixture being *n*-butanol, water, and formic acid (64:25:11), and the spots being located by spraying with sodium hydroxide solution (1 in 10).

B: Mix about 50 mg with about 200 mg of powdered sodium hydroxide, transfer the mixture to a small test tube, heat in a small flame to fusion, and continue the heating for a few minutes longer. Cool, add about 0.5 mL of water, then add a moderate excess of hydrochloric acid, and warm: starch iodate paper placed over the mouth of the test tube turns blue.

Melting range ⟨741⟩: between 162° and 168°.

pH ⟨791⟩: between 4.5 and 5.5, in a solution (1 in 100).

Loss on drying ⟨731⟩—Dry it at 80° under vacuum at a pressure of not more than 5 mm of mercury for 4 hours: it loses not more than 1.0% of its weight.

Limit of keto precursor—Its absorptivity (see *Ultraviolet-Visible Spectroscopy* ⟨857⟩) at 312 nm, determined in a solution in 0.01 N hydrochloric acid containing 2.0 mg per mL, is not more than 0.20.

Assay—

Mobile phase—Prepare a filtered and degassed mixture of 0.1 M sodium sulfate in 0.8% acetic acid. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Transfer about 60 mg of USP Isoetharine Hydrochloride RS, accurately weighed, to a 25-mL volumetric flask, add 4.0 mL of alcohol, and mix. Add 3 drops of 1 N hydrochloric acid, dilute with water to volume, and mix.

Assay preparation—Transfer about 75 mg of Isoetharine Mesylate, accurately weighed, to a 25-mL volumetric flask, add 4.0 mL of alcohol, and mix. Add 3 drops of 1 N hydrochloric acid, dilute with water to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 25-cm column that contains packing L9. The flow rate is about 1.5 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed under *Procedure:* the relative standard deviation for replicate injections is not more than 3.0%.

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 peak responses. Calculate the quantity, in mg, of $C_{13}H_{21}NO_3 \cdot CH_4O_3S$ in the portion of Isoetharine Mesylate taken by the formula:

$$0.025C(335.42 / 275.77)(r_U / r_S)$$

in which C is the concentration, in µg per mL, of USP Isoetharine Hydrochloride RS in the *Standard preparation;* 335.42 and 275.77 are the molecular weights of isoetharine mesylate and isoetharine hydrochloride, respectively; and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Isoetharine Mesylate Inhalation Aerosol

» Isoetharine Mesylate Inhalation Aerosol is a solution of Isoetharine Mesylate in Alcohol in an inert propellant base. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of isoetharine mesylate ($C_{13}H_{21}NO_3 \cdot CH_4O_3S$).

Packaging and storage—Preserve in small, nonreactive, light-resistant, aerosol containers equipped with metered-dose valves and provided with oral inhalation actuators.

USP Reference standards ⟨11⟩—
USP Isoetharine Hydrochloride RS

Identification—

A: Expel a quantity of Inhalation Aerosol, equivalent to about 12 mg of isoetharine mesylate, into 2 mL of methanol, dilute with methanol to 5 mL, and mix: this solution responds to *Identification* test *A* under *Isoetharine Inhalation Solution.*

B: Expel a quantity of Inhalation Aerosol, equivalent to about 12 mg of isoetharine mesylate, into a test tube, evaporate on a steam bath just to dryness, and add 50 mg of powdered sodium hydroxide. Heat in a small flame to fusion, and continue heating for a few seconds longer. Cool, add about 0.5 mL of water, then add a moderate excess of 3 N hydrochloric acid: starch iodate paper placed over the mouth of the test tube turns blue.

Alcohol Determination ⟨611⟩—Weigh accurately a filled Inhalation Aerosol container, and record the weight. Invert the container, and place the outlet tip against the bottom of a 50-mL beaker containing 5 mL of water. Slowly actuate the valve 10 times. Raise the unit above the contents of the beaker, and wash the outlet with 1 mL of water. Collect the washings in the beaker. Dip the outlet stem in alcohol, shake to remove the solvent completely, air-dry the valve, and again weigh the Inhalation Aerosol container. Record the weight of the expelled specimen. Transfer the contents of the beaker, with the aid of 4 mL of water, to a glass-stoppered graduated cylinder. Determine the alcohol content of the test solution thus prepared by the gas-liquid chromatographic procedure, 2 mL of dilute isopropyl alcohol (15 in 100) being used as the internal standard. Calculate the alcohol content of the Inhalation Aerosol taken by the formula:

$$SV / W$$

in which *S* is the percentage (w/v) of alcohol in the test solution; *V* is the total volume, in mL, of the test solution; and *W* is the weight, in g, of the expelled specimen taken: between 25.9% and 35.0% (w/w) of C_2H_5OH is found.

Dose uniformity over the entire contents: meets the requirements for *Metered-Dose Inhalers* under *Aerosols, Nasal Sprays, Metered-Dose Inhalers, and Dry Powder Inhalers* ⟨601⟩.

PROCEDURE FOR DOSE UNIFORMITY—

Ferro-citrate solution and *Buffer solution*—Prepare as directed under *Epinephrine Assay* ⟨391⟩.

Standard preparation—Dissolve an accurately weighed quantity of USP Isoetharine Hydrochloride RS in a freshly prepared sodium bisulfite solution (1 in 1000), and dilute quantitatively and stepwise with the same sodium bisulfite solution as necessary to obtain a solution having a known concentration of about 34 µg per mL.

Test preparation—Discharge the minimum recommended dose into the sampling apparatus and detach the inhaler as directed. Rinse the apparatus (filter and interior) with two 5.0-mL portions of a freshly prepared sodium bisulfite solution (1 in 500), and transfer the resulting solutions quantitatively to a 50-mL centrifuge tube. Add 10 mL of chloroform,