Acceptance criteria: –155° to –165°

• **Loss on Drying** ⟨731⟩
Sample: 100 mg of Ergotamine Tartrate
Analysis: Dry the *Sample* under vacuum at 60° for 4 h.
Acceptance criteria: NMT 5.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed, light-resistant containers in a cold place.

• **USP Reference Standards** ⟨11⟩
USP Ergotamine Tartrate RS

Ergotamine Tartrate Inhalation Aerosol

» Ergotamine Tartrate Inhalation Aerosol is a suspension of microfine Ergotamine Tartrate in propellants in a pressurized container. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of ergotamine tartrate $[(C_{33}H_{35}N_5O_5)_2 \cdot C_4H_6O_6]$.

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

USP Reference standards ⟨11⟩—
USP Ergotamine Tartrate RS

Identification—Place 10 mL of water in a small beaker, and deliver 2 sprays from the Inhalation Aerosol under the surface of the water, actuating the valve by pressing the tip against the bottom of the beaker. To one part of the resulting solution in a test tube add 2 parts of *p*-(dimethylamino)-benzaldehyde TS, and mix: a blue color is produced.

Delivered 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—

Standard preparation—Dissolve an accurately weighed quantity of USP Ergotamine Tartrate RS in a tartaric acid solution (1 in 500), and dilute quantitatively and stepwise with the same tartaric acid solution as necessary to obtain a solution having a known concentration of about 18 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 four 5.0-mL portions of a tartaric acid solution (1 in 500), and transfer the resulting solutions quantitatively to a 50-mL centrifuge tube. Add 10 mL of trichlorotrifluoroethane, insert the stopper, shake vigorously for 1 minute and centrifuge for 5 minutes. Use the clear supernatant as the *Test preparation*.

Procedure—Into three separate flasks transfer 6.0 mL each of the *Test preparation*, the *Standard preparation*, and a tartaric acid solution (1 in 500) to provide the blank. To each flask add 10.0 mL of *p*-dimethylaminobenzaldehyde TS, mix, and allow to stand for 30 minutes. Concomitantly determine the absorbances with a suitable spectrophotometer, in 5-cm cells, of the solutions from the *Test preparation* and the *Standard preparation*, at the wavelength of maximum absorbance at about 546 nm, against the blank. Calculate the quantity, in µg, of $(C_{33}H_{35}N_5O_5)_2.C_4H_6O_6$ contained in the minimum dose taken by the formula:

$$(20CN)(A_U / A_S)$$

in which *C* is the concentration, in µg per mL, of USP Ergotamine Tartrate RS in the *Standard preparation; N* is the number of sprays discharged to obtain the minimum recommended dose; and A_U and A_S are the absorbances of the solutions from the *Test preparation* and the *Standard preparation*, respectively.

Particle size—Prime the valve of the Inhalation Aerosol by alternately shaking and firing it several times through its oral inhalation actuator, and then actuate one measured spray onto a clean, dry microscope slide held 5 cm from the end of the actuator, perpendicular to the direction of the spray. Carefully rinse the slide with about 2 mL of carbon tetrachloride, and allow to dry. Examine the slide under a microscope, equipped with a calibrated ocular micrometer, using 450 × magnification. Focus on the particles of 25 fields of view near the center of the test specimen pattern, and note the size of the great majority of individual particles: they are less than 5 µm in diameter. Record the number and size of all individual crystalline particles (not agglomerates) more than 10 µm in length measured along the longest axis: not more than 10 such particles are observed.

Assay—

Standard preparation—Prepare as directed under *Unit spray content*.

Assay preparation—[NOTE—A suitable specimen beaker is one having a small indentation formed on its inside bottom surface having dimensions adequate to accept the aerosol valve stem during actuation, thereby preventing particle entrapment and side-of-stem leakage during the delivery of the specimen.] Place 10 mL of trichlorotrifluoroethane in a suitable 100-mL beaker. Prime the valve of Ergotamine Tartrate Inhalation Aerosol by alternately shaking and firing it 10 times through its oral inhalation actuator. Accurately weigh the Aerosol, shake it, and immediately deliver a single spray under the surface of the trichlorotrifluoroethane, actuating the valve by pressing the tip into the indentation in the bottom of the beaker. Raise the Aerosol above the surface of the trichlorotrifluoroethane, and shake it gently preparatory to delivering another spray similarly under the surface of the trichlorotrifluoroethane. Deliver a total of 2 sprays in this manner. Rinse the valve stem and ferrule with about 2 mL of trichlorotrifluoroethane, collecting the rinsing with the specimen in the beaker. Allow the Aerosol to dry, weigh it, and determine the total weight of the 2 sprays. Transfer the solution to a centrifuge tube with the aid of two 3-mL portions of trichlorotrifluoroethane, and add 10.0 mL of tartaric acid solution (1 in 500). Insert the stopper, shake vigorously for 15 minutes, centrifuge for 5 minutes, and use the clear supernatant as the *Assay preparation*.

Procedure—Transfer 5.0 mL each of the *Standard preparation*, the *Assay preparation*, and a blank consisting of tartaric acid solution (1 in 500) to separate test tubes. To each tube add 10.0 mL of *p*-dimethylaminobenzaldehyde TS, mix, and allow to stand for 30 minutes. Concomitantly determine the absorbances of the solutions against the blank in 1-cm cells at the wavelength of maximum absorbance at about 546 nm, with a suitable spectrophotometer. Calculate the quantity, in mg, of $(C_{33}H_{35}N_5O_5)_2 \cdot C_4H_6O_6$ in each mL of the Aerosol taken by the formula:

$$(0.01Cd / W)(A_U / A_S)$$

in which *C* is the concentration, in µg per mL, of USP Ergotamine Tartrate RS in the *Standard preparation; d* is the density, in g per mL, of Aerosol determined as directed for *d* in the *Procedure* in the *Assay* under *Isoproterenol Sulfate Inhalation Aerosol; W* is the weight, in g, of the specimen taken; and A_U and A_S are the absorbances of the solutions from the *Assay preparation* and the *Standard preparation*, respectively.