Tolerances—Not less than 75% *(Q)* of the labeled amount of $C_{19}H_{21}N \cdot HCl$ is dissolved in 45 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

PROCEDURE FOR CONTENT UNIFORMITY—

Solution A, Solution B, Mobile phase, Diluent, Standard preparation, and *Chromatographic system*—Proceed as directed in the *Assay.*

Test preparation—Transfer 1 finely powdered Tablet to a 50-mL volumetric flask, add about 1 mL of 2.5 N hydrochloric acid and 5 mL of water for each 5 mg of protriptyline hydrochloride, and shake by mechanical means for 20 minutes or until the Tablet is fully disintegrated. Add 5 mL of alcohol for each 5 mg of protriptyline hydrochloride, and shake for an additional 10 minutes. Dilute with water to volume, mix, and pass through a 0.45-µm membrane filter, discarding the first 1.5 mL of the filtrate. Use the subsequent filtrate as the *Test preparation.*

Procedure—Proceed as directed in the *Assay.* Calculate the quantity, in mg, of protriptyline hydrochloride ($C_{19}H_{21}N \cdot HCl$) in the Tablet taken by the formula:

$$(T C / D)(r_U / r_S)$$

in which T is the labeled quantity, in mg, of protriptyline hydrochloride in the Tablet; C is the concentration, in µg per mL, of USP Protriptyline Hydrochloride RS in the *Standard preparation;* D is the concentration, in µg per mL, of protriptyline hydrochloride in the *Test preparation,* based on the labeled quantity per Tablet and the extent of dilution; and r_U and r_S are the peak responses obtained from the *Test preparation* and the *Standard preparation,* respectively.

Assay—

Solution A—Prepare a filtered and degassed solution of 22.0 g of monobasic sodium phosphate and 3.78 g of sodium 1-hexanesulfonate in 1900 mL of water. Adjust with phosphoric acid to a pH of 2.90, and dilute with water to volume in a 2000-mL volumetric flask. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Solution B—Use filtered and degassed acetonitrile. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Mobile phase—Use variable mixtures of *Solution A* and *Solution B* as directed for *Chromatographic system.*

Diluent—Add 200 mL of alcohol to a 1000-mL volumetric flask. Add 40 mL of 2.5 N hydrochloric acid, dilute with water to volume, and mix.

Standard preparation—Dissolve an accurately weighed quantity of USP Protriptyline Hydrochloride RS in *Diluent,* and dilute quantitatively, and stepwise if necessary, with *Diluent* to obtain a solution having a known concentration of about 0.20 mg per mL.

Assay preparation—Weigh and finely powder not fewer than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 40 mg of protriptyline hydrochloride, to a 200-mL volumetric flask, add 40 mL of alcohol, and shake by mechanical means for 5 minutes. Add 40 mL of water and 8 mL of 2.5 N hydrochloric acid, and shake for an additional 10 minutes. Dilute with water to volume, and mix. Pass through a 0.45-µm membrane filter, discarding the first 5 mL of the filtrate. Use the subsequent filtrate as the *Assay preparation.*

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 280-nm detector and a 4.6-mm × 15-cm column containing 5-µm base-deactivated packing L7. The flow rate is about 1.5 mL per minute. The chromatograph is programmed as follows.

Time (minutes)	*Solution A* (%)	*Solution B* (%)	Elution
0	83	17	equilibration
0–15	83→50	17→50	linear gradient
15–20	50	50	isocratic
20–25	50→83	50→17	linear gradient
25–30	83	17	re-equilibration

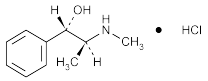
Chromatograph the *Standard preparation* and record the peak responses as directed for *Procedure:* the column efficiency is not less than 25,000 theoretical plates; the tailing factor is not more than 2.5; and the relative standard deviation is not more than 2.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Assay preparation* and the *Standard preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of protriptyline hydrochloride ($C_{19}H_{21}N \cdot HCl$) in the portion of Tablets taken by the formula:

$$200 C(r_U / r_S)$$

in which C is the concentration, in mg per mL, of USP Protriptyline Hydrochloride RS in the *Standard preparation;* and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Pseudoephedrine Hydrochloride



$C_{10}H_{15}NO \cdot HCl$ 201.69

Benzenemethanol, α-[1-(methylamino)ethyl]-, [*S*-(*R**,*R**)]-, hydrochloride.

(+)-Pseudoephedrine hydrochloride [345-78-8].

» Pseudoephedrine Hydrochloride contains not less than 98.0 percent and not more than 102.0 percent of $C_{10}H_{15}NO \cdot HCl$, calculated on the dried basis.

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

USP Reference standards ⟨11⟩**—**
USP Ephedrine Sulfate RS
USP Pseudoephedrine Hydrochloride RS

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: A solution responds to the tests for *Chloride* ⟨191⟩.

Melting range, *Class I* ⟨741⟩: between 182° and 186°, but the range between beginning and end of melting does not exceed 2°.

Specific rotation ⟨781S⟩: between +61.0° and +62.5°.

Test solution: 50 mg per mL, in water.

pH ⟨791⟩: between 4.6 and 6.0, in a solution (1 in 20).

Loss on drying ⟨731⟩**—**Dry it at 105° for 3 hours: it loses not more than 0.5% of its weight.

Residue on ignition ⟨281⟩: not more than 0.1%.

Chromatographic purity—Use the chromatogram of the *Assay preparation,* obtained as directed in the *Assay.* Calculate the percentage of each impurity in the portion of Pseudoephedrine Hydrochloride taken by the formula:

$$100 (r_i / r_s)$$

in which r_i is the response of the individual impurity; and r_s is the sum of all the responses in the chromatogram: the sum of all the impurities found is not more than 2.0%.

Assay—

Triethylamine–phosphoric acid solution—Mix 5 mL of triethylamine with 1 L of water. Adjust with phosphoric acid to a pH of 6.8.

Mobile phase—Prepare a filtered and degassed mixture of *Triethylamine–phosphoric acid solution* and methanol (90:10). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

System suitability solution—Prepare a solution in water containing about 0.1 mg of USP Pseudoephedrine Hydrochloride RS and 0.002 mg of USP Ephedrine Sulfate RS per mL.

Standard preparation—Dissolve an accurately weighed quantity of USP Pseudoephedrine Hydrochloride RS in water to obtain a solution having a known concentration of about 0.1 mg per mL.

Assay preparation—Transfer about 100 mg of Pseudoephedrine Hydrochloride, accurately weighed, to a 100-mL volumetric flask, and dissolve in and dilute with water to volume. Dilute the solution, stepwise if necessary, to obtain a final concentration of 0.1 mg per mL.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 206-nm detector and a 3.0-mm × 15-cm column that contains packing L11. The flow rate is about 0.6 mL per minute. Chromatograph the *System suitability solution,* and record the peak responses as directed for *Procedure:* the relative retention times are about 0.9 for ephedrine and 1.0 for pseudoephedrine; the resolution, *R,* between the pseudoephedrine and ephedrine peaks is not less than 2.0; the tailing factor for the pseudoephedrine peak is not more than 2.0; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Assay preparation* and the *Standard preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the percentage of $C_{10}H_{15}NO \cdot HCl$, in the portion of Pseudoephedrine Hydrochloride taken by the formula:

$$100\,(C_S / C_U)(r_U / r_S)$$

in which C_S and C_U are the concentrations, in mg per mL, of pseudoephedrine hydrochloride in the *Standard preparation* and *Assay preparation,* respectively; and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Dissolution ⟨711⟩**—**

Medium: water; 900 mL.

Apparatus 2: 50 rpm.

Times: 3, 6, and 12 hours.

Procedure—Determine the amount of $C_{10}H_{15}NO \cdot HCl$ dissolved, employing the procedure set forth in the *Assay,* using a filtered portion of the solution under test as the *Assay preparation* in comparison with a Standard solution having a known concentration of USP Pseudoephedrine Hydrochloride RS in the same *Medium.*

Tolerances—The percentages of the labeled amount of $C_{10}H_{15}NO \cdot HCl$ dissolved at the times specified conform to *Acceptance Table 2.*

Time (hours)	Amount dissolved
3	between 20% and 50%
6	between 45% and 75%
12	not less than 75%

Uniformity of dosage units ⟨905⟩**:** meet the requirements.

Assay—

Mobile phase, Standard preparation, and *Chromatographic system*—Proceed as directed in the *Assay* under *Pseudoephedrine Hydrochloride Extended-Release Tablets*.

Assay preparation—Remove, as completely as possible, the contents of not fewer than 20 Capsules, weigh, and mix. Transfer an accurately weighed portion of the combined contents, equivalent to about 120 mg of pseudoephedrine hydrochloride, to a 100-mL volumetric flask, add 10 mL of 0.01 N hydrochloric acid, and sonicate for 10 minutes. Cool to room temperature. Dilute with 0.01 N hydrochloric acid to volume, mix, and filter.

Procedure—Proceed as directed in the *Assay* under *Pseudoephedrine Hydrochloride Extended-Release Tablets*. Calculate the quantity, in mg, of pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) in the portion of Capsules taken by the formula:

$$100C(r_U / r_S)$$

in which C is the concentration, in mg per mL, of USP Pseudoephedrine Hydrochloride RS in the *Standard preparation;* and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Pseudoephedrine Hydrochloride Extended-Release Capsules

» Pseudoephedrine Hydrochloride Extended-Release Capsules contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$).

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩**—**
USP Pseudoephedrine Hydrochloride RS

Identification—

A: A portion of Capsule contents, equivalent to about 180 mg of pseudoephedrine hydrochloride, meets the requirements of *Identification* test *A* under *Pseudoephedrine Hydrochloride Extended-Release Tablets*.

B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay*.

Pseudoephedrine Hydrochloride Oral Solution

» Pseudoephedrine Hydrochloride Oral Solution contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$).

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

USP Reference standards ⟨11⟩**—**
USP Pseudoephedrine Hydrochloride RS

Identification—Extract a volume of Oral Solution, equivalent to about 120 mg of pseudoephedrine hydrochloride, with two 30-mL portions of ether, discard the extracts, and add 4 mL of 1 N sodium hydroxide. Extract with 30 mL of chloroform, and evaporate the chloroform on a steam bath, avoiding overheating: the pseudoephedrine so obtained melts at about 118°, the procedure for *Class I* being used (see *Melting Range or Temperature* ⟨741⟩), and when 50 mg is dissolved in 10 mL of 0.1 N hydrochloric acid, the resulting solution is dextrorotatory.