monium molybdate solution (1 in 10), which previously had been filtered if necessary. Add 20 mL of 1 N sulfuric acid, dilute with water to volume, and mix.

Acidity—Dissolve 5.0 g in 50 mL of carbon dioxide-free water, add 3 drops of phenolphthalein TS, and titrate with 0.020 N sodium hydroxide to a distinct pink endpoint: not more than 0.30 mL of 0.020 N sodium hydroxide is required for neutralization.

Loss on drying ⟨731⟩—Dry it at 105° for 4 hours: it loses not more than 0.3% of its weight.

Chloride ⟨221⟩—A 2.0-g portion shows no more chloride than corresponds to 0.20 mL of 0.020 N hydrochloric acid (0.007%).

Sulfate ⟨221⟩—A 2.0-g portion shows no more sulfate than corresponds to 0.20 mL of 0.020 N sulfuric acid (0.01%).

Arsenic, *Method II* ⟨211⟩: 1 ppm.

Reducing sugars—To 5 mL of alkaline cupric citrate TS add 1 mL of a saturated solution of Mannitol (about 200 mg). Heat for 5 minutes in a boiling water bath: not more than a very slight precipitate is formed. The amount determined in this test is not included in the calculated amount under *Other Impurities.*

Assay—

Mobile phase—Use degassed water.

Resolution solution—Dissolve sorbitol and USP Mannitol RS in water to obtain a solution having concentrations of about 4.8 mg per mL of each.

Standard preparation—Dissolve an accurately weighed quantity of USP Mannitol RS in water, and dilute quantitatively with water to obtain a solution having a known concentration of about 4.8 mg per mL.

Assay preparation—Transfer about 0.24 g of Mannitol, accurately weighed, to a 50-mL volumetric flask, dissolve in 10 mL of water, dilute with water to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a refractive index detector that is maintained at a constant temperature and a 4-mm × 25-cm column that contains packing L19. The column temperature is maintained at a temperature between 30° and 85° controlled within ±2° of the selected temperature, and the flow rate is about 0.5 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 2.0%. In a similar manner, chromatograph the *Resolution solution:* the resolution, *R,* between the sorbitol and mannitol peaks is not less 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 $C_6H_{14}O_6$, in the Mannitol taken by the formula:

$$50C(r_U / r_S)$$

in which C is the concentration, in mg per mL, of USP Mannitol 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.

Mannitol Injection

» Mannitol Injection is a sterile solution, which may be supersaturated, of Mannitol in Water for Injection. It may require warming or autoclaving before use if crystallization has occurred. It contains not less than 95.0 percent and not more than 105.0 percent of the labeled amount of mannitol ($C_6H_{14}O_6$). It contains no antimicrobial agents.

Packaging and storage—Preserve in single-dose glass or plastic containers. Glass containers are preferably of Type I or Type II glass.

Labeling—The label states the total osmolar concentration in mOsmol per L. Where the contents are less than 100 mL, or where the label states that the Injection is not for direct injection but is to be diluted before use, the label alternatively may state the total osmolar concentration in mOsmol per mL. The label also states that it should be warmed before use to dissolve any crystals that may have formed.

USP Reference standards ⟨11⟩—
USP Endotoxin RS
USP Mannitol RS

Identification—

A: Evaporate a portion of Injection on a steam bath to dryness, and dry the residue at 105° for 4 hours. To 3 mL of freshly prepared solution of catechol in water (1 in 10) add 6 mL of sulfuric acid with cooling. Place 3 mL of this solution in each of two separate test tubes. To one tube add 0.3 mL of water (reagent blank) and to the other add 0.3 mL of a solution of it in water (1 in 10). Heat the tubes over an open flame for about 30 seconds: the solution in the tube containing mannitol is dark pink or wine red, and the solution in the tube containing the reagent blank is light pink.

B: The retention time for 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.*

Specific rotation ⟨781⟩—Transfer an accurately measured volume of Injection, equivalent to about 1 g of mannitol as determined by the *Assay*, to a 100-mL volumetric flask: it meets the requirements of the test for *Specific rotation* under *Mannitol.*

Bacterial endotoxins ⟨85⟩—It contains not more than 0.04 USP Endotoxin Unit per mg of mannitol where the labeled amount of mannitol in the Injection is 10% or less, and not more than 2.5 USP Endotoxin Units per g of mannitol where the labeled amount of mannitol in the Injection is greater than 10%.

pH ⟨791⟩**:** between 4.5 and 7.0, determined potentiometrically, on a portion to which 0.30 mL of saturated potassium chloride solution has been added for each 100 mL, and which previously has been diluted with water, if necessary, to a concentration of not more than 5% of mannitol.

Particulate matter ⟨788⟩**:** meets the requirements for small-volume injections.

Other requirements—It meets the requirements under *Injections* ⟨1⟩.

Assay—

Mobile phase, Resolution solution, and *Chromatographic system*—Proceed as directed in the *Assay* under *Mannitol.*

Standard preparation—Dissolve an accurately weighed quantity of USP Mannitol RS in water, and dilute quantitatively with water to obtain a solution having a known concentration of about 5 mg per mL.

Assay preparation—Transfer an accurately measured volume of Injection, equivalent to about 500 mg of mannitol, to a 100-mL volumetric flask, dilute with water to volume, and mix.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Mannitol*. Calculate the quantity, in mg, of mannitol ($C_6H_{14}O_6$) in each mL of the Injection taken by the formula:

$$100(C/V)(r_U / r_S)$$

in which *V* is the volume, in mL, of Injection taken; and the other terms are as defined therein.

Mannitol in Sodium Chloride Injection

» Mannitol in Sodium Chloride Injection is a sterile solution of Mannitol and Sodium Chloride in Water for Injection. It contains not less than 95.0 percent and not more than 105.0 percent of the labeled amounts of $C_6H_{14}O_6$ and NaCl. It contains no antimicrobial agents.

Labeling—The label states the total osmolar concentration in mOsmol per L. Where the contents are less than 100 mL, or where the label states that the Injection is not for direct injection but is to be diluted before use, the label alternatively may state the total osmolar concentration in mOsmol per mL.

USP Reference standards ⟨11⟩—
USP Endotoxin RS
USP Mannitol RS

Identification—

A: Evaporate a portion of Injection on a steam bath to dryness, and dry the residue at 105° for 4 hours: the residue responds to the *Identification* test *A* under *Mannitol Injection*.

B: It responds to the tests for *Sodium* ⟨191⟩ and for *Chloride* ⟨191⟩.

Bacterial endotoxins ⟨85⟩—It contains not more than 0.04 USP Endotoxin Unit per mg of mannitol.

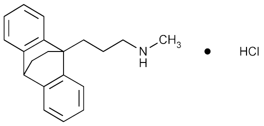
pH ⟨791⟩: between 4.5 and 7.0.

Other requirements—It meets the requirements for *Packaging and storage* under *Mannitol Injection*. It meets also the requirements under *Injections* ⟨1⟩.

Assay for mannitol—Proceed with Injection as directed in the *Assay* under *Mannitol Injection*.

Assay for sodium chloride—Proceed with Injection as directed in the *Assay* under *Sodium Chloride Injection*.

Maprotiline Hydrochloride



$C_{20}H_{23}N \cdot HCl$ 313.86

9,10-Ethanoanthracene-9(10*H*)-propanamine, *N*-methyl-, hydrochloride.

N-Methyl-9,10-ethanoanthracene-9(10*H*)-propylamine hydrochloride [10347-81-6].

» Maprotiline Hydrochloride contains not less than 99.0 percent and not more than 101.0 percent of the labeled amount of $C_{20}H_{23}N \cdot HCl$, calculated on the dried basis.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—
USP Maprotiline Hydrochloride RS

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 100 µg per mL.

Medium: methanol.

Absorptivities at 266 nm and 272 nm, calculated on the dried basis, do not differ by more than 3.0%.

C: A solution (1 in 200) responds to the tests for *Chloride* ⟨191⟩, when tested as specified for alkaloidal hydrochlorides.

Loss on drying ⟨731⟩—Dry it in vacuum at 80° to constant weight: it loses not more than 1.0% of its weight.

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

Heavy metals, *Method II* ⟨231⟩: 0.001%.

Chromatographic purity—

Standard solutions—Dissolve USP Maprotiline Hydrochloride RS in methanol, and mix to obtain a stock standard solution having a known concentration of 20 mg per mL. Dilute quantitatively with methanol to obtain *Standard solution* having a known concentration of 0.10 mg per mL. Dilute quantitatively with methanol to obtain *Standard solutions*, designated below by letter, having the following compositions:

Standard solution	Dilution	Concentration (µg RS per mL)	Percentage (%, for comparison with test specimen)
A	(undiluted)	100	0.5
B	(4 in 5)	80	0.4
C	(3 in 5)	60	0.3
D	(2 in 5)	40	0.2
E	(1 in 5)	20	0.1

Test solution—Dissolve an accurately weighed quantity of Maprotiline Hydrochloride in methanol to obtain a solution containing 20 mg per mL.

Procedure—In a suitable chromatographic chamber (see *Chromatography* ⟨621⟩), place a volume of a solvent system consisting of a mixture of secondary butyl alcohol, ethyl acetate, and 2 N ammonium hydroxide (6:3:1) sufficient to develop a chromatogram. Place a beaker containing 25 mL of ammonium hydroxide in the bottom of the chamber, and allow it to equilibrate for 1 hour. Apply 5-µL portions of the *Test solution*, the stock standard solution, and each of the *Standard solutions* to a suitable thin-layer chromatographic plate coated with a 0.25-mm layer of chromatographic silica gel that has been pre-washed with chloroform by allowing chloroform to move the full length of the plate, and dried at 100° for 30 minutes, and allow the spots to dry. Develop the chromatograms until the solvent front has moved about three-fourths of the length of the plate, remove the plate from the developing chamber, mark the solvent front, and allow the solvent to evaporate. Expose the plate to hydrogen chloride vapor for 30 minutes, expose it to a high-intensity UV light irradiator (1000 to 1600 watts) [*Caution—UV irradiators emit UV radiation that is harmful to eyes and skin.]* until the spot in the chromatogram of *Standard solution E* is clearly visible, and compare the chromatograms under long-wavelength UV light: the R_F value of the principal spot obtained from the *Test solution* corresponds to that obtained from the stock standard solution; and the sum of the intensities of all secondary spots obtained from the *Test solution,* compared with those of the principal spots obtained from the *Standard solutions,* corresponds to not more than 1.0%.

Assay—Dissolve about 600 mg of Maprotiline Hydrochloride, accurately weighed, in 25 mL of mercuric acetate TS, and titrate with 0.1 N perchloric acid VS, determining the endpoint potentiometrically, using a glass electrode and a calomel electrode containing saturated lithium chloride in glacial acetic acid (see *Titrimetry* ⟨541⟩). Perform a blank determination, and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 31.39 mg of $C_{20}H_{23}N \cdot HCl$.

Maprotiline Hydrochloride Tablets

» Maprotiline Hydrochloride Tablets contain not less than 90.0 percent and not more than 110.0