2000

USP 24
NF 19

THE UNITED STATES PHARMACOPEIA

THE NATIONAL FORMULARY

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Vol. 2

UNITED STATES PHARMACOPEIAL CONVENTION, INC.
12601 Twinbrook Parkway, Rockville, MD 20852

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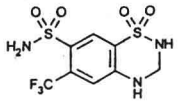
Hydroflumethiazide



$C_8H_8F_3N_3O_4S_2$ 331.29

2*H*-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-6-(trifluoromethyl)-, 1,1-dioxide.

3,4-Dihydro-6-(trifluoromethyl)-2*H*-1,2,4-benzothiadiazine-7-sulfonamide 1,1-dioxide [*135-09-1*].

» Hydroflumethiazide contains not less than 98.0 percent and not more than 102.0 percent of $C_8H_8F_3N_3O_4S_2$, calculated on the anhydrous basis.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—*USP Hydroflumethiazide RS. USP 2,4-Disulfamyl-5-trifluoromethylaniline RS.*

Identification—

A: *Infrared Absorption* ⟨197K⟩, previously dried over silica gel for 4 hours.

B: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 10 μg per mL.

Medium: methanol.

Melting range, *Class I* ⟨741⟩: between 270° and 275°.

pH ⟨791⟩: between 4.5 and 7.5, in a 1 in 100 dispersion in water.

Water, *Method I* ⟨921⟩: not more than 1.0%.

Residue on ignition ⟨281⟩: not more than 1.0%.

Heavy metals, *Method II* ⟨231⟩: 0.002%.

Selenium ⟨291⟩: 0.003%.

Diazotizable substances—

Standard preparation—Transfer 10.0 mg of USP 2,4-Disulfamyl-5-trifluoromethylaniline RS to a 50-mL volumetric flask, dissolve in and dilute with acetone to volume, and mix. Transfer 10.0 mL of this solution to a 100-mL volumetric flask, dilute with water to volume, and mix.

Test preparation—Transfer 100 mg to a 50-mL volumetric flask, dissolve in 5 mL of acetone, dilute with water to volume, and mix.

Procedure—Transfer 5.0 mL each of the *Standard preparation*, the *Test preparation*, and a solution of acetone in water (1 in 10) to provide the blank, to separate 25-mL volumetric flasks. To each flask add 2.0 mL of dilute hydrochloric acid (1 in 5), and immediately add 1 mL of freshly prepared sodium nitrite solution (1 in 100). Mix, and allow to stand for 5 minutes. Add 1 mL of freshly prepared ammonium sulfamate solution (1 in 10) to each flask, mix, and allow to stand for 1 minute, with frequent swirling. Add 1 mL of a freshly prepared solution of *N*-(1-naphthyl)ethylenediamine dihydrochloride (1 in 1000), and mix. After 1 minute, dilute with water to volume, and mix. Concomitantly, and within 5 minutes after mixing, taking care to establish the same elapsed time for each solution, determine the absorbances of the solutions in 1-cm cells at 518 nm, with a suitable spectrophotometer, using the blank to set the instrument: the absorbance of the solution from the *Test preparation* does not exceed that of the solution from the *Standard preparation*, corresponding to not more than 1.0% of diazotizable substances.

Organic volatile impurities, *Method V* ⟨467⟩: meets the requirements.

Solvent—Use dimethyl sulfoxide as the solvent.

Assay—Transfer about 50 mg of Hydroflumethiazide, accurately weighed, to a 100-mL volumetric flask, add methanol to volume, and mix. Transfer 2.0 mL of this solution to a second 100-mL volumetric flask, dilute with methanol to volume, and mix. Concomitantly determine the absorbances of this solution and a Standard solution of USP Hydroflumethiazide RS in the same medium having a known concentration of about 10 μg per mL, in 1-cm cells at the wavelength of maximum absorbance at about 273 nm, with a suitable spectrophotometer, using methanol as the blank. Calculate the quantity, in mg, of $C_8H_8F_3N_3O_4S_2$ in the Hydroflumethiazide taken by the formula:

$$5C(A_U/A_S),$$

in which C is the concentration, in μg per mL, of USP Hydroflumethiazide RS in the Standard solution, and A_U and A_S are the absorbances of the solution of Hydroflumethiazide and the Standard solution, respectively.

Hydroflumethiazide Tablets

» Hydroflumethiazide Tablets contain not less than 95.0 percent and not more than 105.0 percent of the labeled amount of $C_8H_8F_3N_3O_4S_2$.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—*USP Hydroflumethiazide RS.*

Identification—Finely powder a number of Tablets, equivalent to about 100 mg of hydroflumethiazide, and place the powder in a 35-mL, screw-capped centrifuge tube. Add 30 mL of acetone, cap the tube, and allow it to stand for 30 minutes, with occasional shaking. Centrifuge, and decant the supernatant liquid into a 100-mL beaker. Evaporate on a steam bath to dryness, add 10 mL of sodium hydroxide solution (1 in 250) to the residue, and mix. Transfer the liquid to a 125-mL separator. Rinse the beaker with 5 mL of water, and add the rinsing to the main portion. Add 50 mL of anhydrous ethyl ether to the separator, insert the stopper, shake vigorously for 2 minutes, releasing pressure as necessary, and allow the phases to separate. Draw off the lower phase, retaining any emulsion in the separator, and filter it through a membrane filter of 0.2- to 2-μm pore size. Add dilute hydrochloric acid (1 in 10) dropwise to the filtrate in a 50-mL beaker, stirring well and checking the pH with wide-range test paper after each drop. [NOTE—Crystallization begins at about pH 5. Rubbing the bottom of the beaker with a glass stirring rod helps to initiate crystallization.] When precipitation is complete, decant and discard the supernatant liquid, and wash the precipitate with 5 mL of water. Decant and discard the wash water, and dry the precipitate at 105° for 30 minutes: the infrared spectrum of a potassium bromide dispersion of the dried material exhibits maxima only at the same wavelengths as that of a similar preparation of USP Hydroflumethiazide RS.

Dissolution ⟨711⟩—

Medium: dilute hydrochloric acid (1 in 100); 900 mL.

Apparatus 2: 50 rpm.

Time: 60 minutes.

Procedure—Determine the amount of $C_8H_8F_3N_3O_4S_2$ dissolved from ultraviolet absorbances at the wavelength of maximum absorbance at about 273 nm of filtered portions of the solution under test, suitably diluted with *Dissolution Medium*, if necessary, in comparison with a Standard solution having a known concentration of USP Hydroflumethiazide RS in the same medium.

Tolerances—Not less than 80% (Q) of the labeled amount of $C_8H_8F_3N_3O_4S_2$ is dissolved in 60 minutes.

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

Procedure for content uniformity—Crush 1 Tablet and transfer quantitatively to a 100-mL volumetric flask, add about 50-mL of methanol, and shake until disintegration is complete. Dilute with methanol to volume, mix, and filter, discarding the first 20 mL of the filtrate. Dilute a portion of the subsequent filtrate with methanol to obtain a solution containing approximately 10 μg of hydroflumethiazide per mL. Concomitantly determine the absorbances of this solution and of a Standard solution of USP Hydroflumethiazide RS, in the same medium having a known concentration of about 10 μg per mL in 1-cm cells at the wavelength of maximum absorbance at about 273 nm, with a suitable spectrophotometer, using methanol as the blank. Calculate the quantity, in mg, of $C_8H_8F_3N_3O_4S_2$ in the Tablet taken by the formula:

$$(TC/D)(A_U/A_S),$$

in which T is the labeled quantity, in mg, of hydroflumethiazide in the Tablet, C is the concentration, in μg per mL, of USP Hydroflumethiazide RS in the Standard solution, D is the concentration, in μg per mL, of hydroflumethiazide in the test solution, based upon

the labeled quantity per Tablet and the extent of dilution, and A_U and A_S are the absorbances of the solution from the Tablet and the Standard solution, respectively.

Assay—

Standard preparation—Transfer about 30 mg of USP Hydroflumethiazide RS, accurately weighed, to a 100-mL volumetric flask, add sodium hydroxide solution (1 in 100) to volume, and mix. Transfer 5.0 mL of this solution to a second 100-mL volumetric flask, dilute with sodium hydroxide solution (1 in 100) to volume, and mix. The concentration of USP Hydroflumethiazide RS in the *Standard preparation* is about 15 µg per mL.

Chromatographic column—Proceed as directed for *Column Partition Chromatography* under *Chromatography* ⟨621⟩, packing a chromatographic tube with two segments of packing material. The lower segment is a mixture of 1 g of *Solid Support* and 1 mL of sodium hydroxide solution (1 in 100), and the upper segment is a mixture prepared as directed under *Assay preparation*.

Assay preparation—Weigh and finely powder not less than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 75 mg of hydroflumethiazide, to a 50-mL volumetric flask, add about 35 mL of sodium hydroxide solution (1 in 100), shake vigorously, dilute with sodium hydroxide solution (1 in 100) to volume, and mix. Mix 2.0 mL of this solution with 3 g of *Solid Support* as directed under *Chromatographic column*, and transfer to the column. Wash the column with 50 mL of water-saturated chloroform, then with 50 mL of water-saturated ether, and discard the eluates. Elute the hydroflumethiazide from the column with 100 mL of glacial acetic acid in ether (1 in 1000), collecting the eluate in a 250-mL separator. Add 100 mL of a 1 in 1000 solution of glacial acetic acid in ether to a second 250-mL separator to provide a blank, and treat each as follows: Add 60 mL of isooctane to each separator, mix, and extract the resulting solution with three 50-mL portions of sodium hydroxide solution (1 in 100), collecting the extracts in a 200-mL volumetric flask. Dilute with sodium hydroxide solution (1 in 100) to volume, and mix.

Procedure—Concomitantly determine the absorbances of the solutions in 1-cm cells at the wavelength of maximum absorbance at about 273 nm, with a suitable spectrophotometer, using the blank. Calculate the quantity, in mg, of $C_8H_8F_3N_3O_4S_2$ in the portion of Tablets taken by the formula:

$$5C(A_U/A_S),$$

in which C is the concentration, in µg per mL, of USP Hydroflumethiazide RS in the *Standard preparation*, and A_U and A_S are the absorbances of the *Assay preparation* and the *Standard preparation*, respectively.

Hydrogen Peroxide Concentrate

H_2O_2 34.01
Hydrogen peroxide.
Hydrogen peroxide [*7722-84-1*].

» Hydrogen Peroxide Concentrate contains not less than 29.0 percent and not more than 32.0 percent, by weight, of H_2O_2. It contains not more than 0.05 percent of a suitable preservative or preservatives. *Caution—Hydrogen Peroxide Concentrate is a strong oxidant.*

Packaging and storage—Preserve in partially-filled containers having a small vent in the closure, and store in a cool place.

Labeling—Label it to indicate the name and amount of any added preservative.

Acidity—Dilute 25 g with water to 250 mL, add phenolphthalein TS, and titrate with 0.10 *N* sodium hydroxide: not more than 2.5 mL is required for neutralization.

Chloride ⟨221⟩—1.5 g diluted with water to 25 mL shows no more chloride than 0.10 mL of 0.020 *N* hydrochloric acid (0.005%).

Other requirements—It responds to the *Identification* test and meets the requirements of the tests for *Nonvolatile residue*, *Heavy metals*, and *Limit of preservative* (90 mL of it being used) under *Hydrogen Peroxide Topical Solution*.

Assay—Weigh accurately about 1 mL of Concentrate in a tared 100-mL volumetric flask, dilute with water to volume, and mix. To 20.0 mL of this solution add 20 mL of 2 *N* sulfuric acid, and titrate with 0.1 *N* potassium permanganate VS. Each mL of 0.1 *N* potassium permanganate is equivalent to 1.701 mg of H_2O_2.

Hydrogen Peroxide Topical Solution

H_2O_2 34.01
Hydrogen peroxide.
Hydrogen peroxide [*7722-84-1*].

» Hydrogen Peroxide Topical Solution contains, in each 100 mL, not less than 2.5 g and not more than 3.5 g of H_2O_2. It contains not more than 0.05 percent of a suitable preservative or preservatives.

Packaging and storage—Preserve in tight, light-resistant containers, at controlled room temperature.

Identification—Shake 1 mL with 10 mL of water containing 1 drop of 2 *N* sulfuric acid, and add 2 mL of ether: the subsequent addition of a drop of potassium dichromate TS produces an evanescent blue color in the water layer which upon agitation and standing passes into the ether layer.

Acidity—To 25 mL add phenolphthalein TS, and titrate with 0.10 *N* sodium hydroxide: not more than 2.5 mL is required for neutralization.

Barium—To 10 mL add two drops of 2 *N* sulfuric acid: no turbidity or precipitate is produced within 10 minutes.

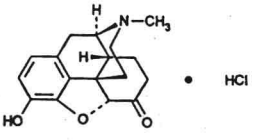
Heavy metals ⟨231⟩—Dilute 4 mL, previously shaken, with 20 mL of water, add 2 mL of 6 *N* ammonium hydroxide, and gently boil the solution until the volume is reduced to about 5 mL. Dilute with water to 25 mL: the limit is 5 ppm.

Limit of nonvolatile residue—Evaporate 20 mL, previously shaken, on a steam bath to dryness, and dry the residue at 105° for 1 hour: the weight of the residue does not exceed 30 mg.

Limit of preservative—Extract 100 mL of well-mixed Topical Solution in a separator with a mixture of 3 volumes of chloroform and 2 volumes of ether, using 50 mL, 25 mL, and 25 mL, respectively. Evaporate the combined extracts at room temperature in a tared glass dish to dryness, and dry over silica gel for 2 hours: the residue, if any, weighs not more than 50 mg (0.05%).

Assay—Pipet 2 mL of Topical Solution into a suitable flask containing 20 mL of water. Add 20 mL of 2 *N* sulfuric acid, and titrate with 0.1 *N* potassium permanganate VS. Each mL of 0.1 *N* potassium permanganate is equivalent to 1.701 mg of H_2O_2.

Hydromorphone Hydrochloride



$C_{17}H_{19}NO_3 \cdot HCl$ 321.80
Morphinan-6-one, 4,5-epoxy-3-hydroxy-17-methyl-, hydrochloride, (5α)-.
4,5α-Epoxy-3-hydroxy-17-methylmorphinan-6-one hydrochloride [*71-68-1*].

» Hydromorphone Hydrochloride, dried at 105° for 2 hours, contains not less than 98.0 percent and not more than 101.0 percent of $C_{17}H_{19}NO_3 \cdot HCl$.

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

USP Reference standards ⟨11⟩—*USP Hydromorphone Hydrochloride RS.*

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 100 µg per mL.

Medium: water. Absorptivities at 280 nm, calculated on the dried basis, do not differ by more than 3.0%.

C: A solution (1 in 20) responds to the tests for *Chloride* ⟨191⟩.

Specific rotation ⟨781S⟩: between −136° and −139°.

Test solution: 50 mg per mL, in water.

Acidity—Dissolve 300 mg in 10 mL of water, add 1 drop of methyl red TS, and titrate with 0.020 *N* sodium hydroxide VS: not more than 0.30 mL is required to produce a yellow color.

Loss on drying ⟨731⟩—Dry it at 105° for 2 hours: it loses not more than 1.5% of its weight.

Residue on ignition ⟨281⟩: not more than 0.3%.

Sulfate—To a solution of 100 mg in 5 mL of water add 0.5 mL of 3 *N* hydrochloric acid and 1 mL of barium chloride TS: no turbidity is produced.

Ordinary impurities ⟨466⟩—

Test solution: water.

Standard solution: water.

Eluant: a mixture of methylene chloride, methanol, and ammonium hydroxide (80:20:1).

Visualization: 3, followed by overspraying with hydrogen peroxide TS and exposure of the plate to iodine vapors for about 30 minutes.

Organic volatile impurities, *Method I* ⟨467⟩: meets the requirements.

Assay—Transfer about 225 mg of Hydromorphone Hydrochloride, previously dried and accurately weighed, to a 250-mL conical flask, and dissolve in 80 mL of glacial acetic acid, warming, if necessary. Cool, and add 5 mL of acetic anhydride and 10 mL of mercuric acetate TS. Add 1 drop of crystal violet TS, and titrate with 0.1 *N* perchloric acid VS to a blue endpoint. Perform a blank determination, and make any necessary correction. Each mL of 0.1 *N* perchloric acid is equivalent to 32.18 mg of $C_{17}H_{19}NO_3 \cdot HCl$.

Hydromorphone Hydrochloride Injection

» Hydromorphone Hydrochloride Injection is a sterile solution of Hydromorphone Hydrochloride in Water for Injection. It contains not less than 95.0 percent and not more than 105.0 percent of the labeled amount of $C_{17}H_{19}NO_3 \cdot HCl$.

Packaging and storage—Preserve in single-dose or in multiple-dose containers, preferably of Type I glass, protected from light.

USP Reference standards ⟨11⟩—*USP Hydromorphone Hydrochloride RS. USP Endotoxin RS.*

Identification—Place a volume of Injection, equivalent to about 10 mg of hydromorphone hydrochloride, in a separator. Extract with four 10-mL portions of chloroform, and discard the extracts. Add 1 mL of sodium carbonate TS, and extract with three 10-mL portions of chloroform. Filter the chloroform extracts into a glass-stoppered, 50-mL flask, and evaporate on a steam bath with the aid of a current of air to dryness. Dissolve the residue in 1 mL of chloroform: the infrared absorption spectrum of the solution so obtained exhibits maxima only at the same wavelengths as that of a similar preparation of USP Hydromorphone Hydrochloride RS.

Bacterial endotoxins ⟨85⟩—It contains not more than 88.0 USP Endotoxin Units per mg of hydromorphone hydrochloride.

pH ⟨791⟩: between 3.5 and 5.5.

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

Assay—

Standard preparation—Using an accurately weighed quantity of USP Hydromorphone Hydrochloride RS, prepare a solution in water having a known concentration of about 0.2 mg per mL.

Assay preparation—Quantitatively dilute an accurately measured volume of Injection, if necessary, with water to obtain a solution containing about 0.2 mg per mL.

Procedure—Transfer 20.0 mL each of the *Standard preparation* and the *Assay preparation* to separate 50-mL volumetric flasks. To each flask add, with mixing, 1.0 mL of hydrochloric acid and 1.0 mL of sodium nitrite solution (1 in 20). Insert the stoppers, allow to stand for 40 to 45 minutes, with occasional swirling, then add 2 mL of ammonium hydroxide, and mix. Allow to stand for 2 minutes, then dilute with water to volume, and mix. Concomitantly determine the absorbances of the solutions in 1-cm cells at the wavelength of maximum absorbance at about 440 nm, with a suitable spectrophotometer, using water as the blank. Calculate the quantity, in mg, of $C_{17}H_{19}NO_3 \cdot HCl$ in each mL of the Injection taken by the formula:

$$(V_A/V_I)(C)(A_U/A_S),$$

in which V_A is the volume, in mL, of the *Assay preparation*, V_I is the volume, in mL, of Injection taken to prepare the *Assay preparation*, C is the concentration, in mg per mL, of USP Hydromorphone Hydrochloride RS in the *Standard preparation*, and A_U and A_S are the absorbances of the solutions from the *Assay preparation* and the *Standard preparation*, respectively.

Hydromorphone Hydrochloride Tablets

» Hydromorphone Hydrochloride Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{17}H_{19}NO_3 \cdot HCl$.

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

USP Reference standards ⟨11⟩—*USP Hydromorphone Hydrochloride RS.*

Identification—Place a quantity of finely powdered Tablets, equivalent to about 10 mg of hydromorphone hydrochloride, in a separator, and proceed as directed in the *Identification* test under *Hydromorphone Hydrochloride Injection*, beginning with "Extract with four 30-mL portions of chloroform."

Dissolution ⟨711⟩—

Medium: water; 500 mL.

Apparatus 2: 50 rpm.

Time: 45 minutes.

Standard preparation—Dissolve an accurately weighed quantity of USP Hydromorphone Hydrochloride RS in *Dissolution Medium*, and dilute quantitatively with *Dissolution Medium* to obtain a solution having a known concentration of about 0.10 mg per mL.

Procedure—Pipet into each of two separate containers a volume of a filtered portion of the solution under test that is estimated to contain about 0.1 mg of hydromorphone hydrochloride and add water, if necessary, to bring each to a volume of 50.0 mL. Label one container as the test solution and one as the Test blank. Pipet 1 mL of the *Standard preparation* into each of two separate containers, and add water to bring each to a volume of 50.0 mL. Label one container as the Standard solution and one as the Standard blank. Add 4.0 mL of 1.0 *N* hydrochloric acid to all four containers, and add 1.0 mL of sodium nitrite solution (1 in 20) to the test solution and the Standard solution. Mix, and allow to stand for 15 minutes, accurately timed. Add 2.0 mL of ammonium hydroxide to each of the four containers, mix, and determine the absorbances of the solutions at the wavelength of maximum absorbance at about 440 nm. Calculate the amount of hydromorphone hydrochloride dissolved by comparison of the absorbances obtained from the test

solution and the Standard solution, using the respective blank solutions to correct the absorbances.

Tolerances—Not less than 75% (*Q*) of the labeled amount of $C_{17}H_{19}NO_3 \cdot HCl$ is dissolved in 45 minutes.

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

Assay—

Standard preparation—Dissolve an accurately weighed quantity of USP Hydromorphone Hydrochloride RS in water to obtain a solution having a known concentration of about 1 mg per mL.

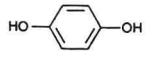
Assay preparation—Weigh and finely powder not less than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 50 mg of hydromorphone hydrochloride, to a 50-mL volumetric flask, add water to volume, mix, and filter.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Hydromorphone Hydrochloride Injection*. Calculate the quantity, in mg, of $C_{17}H_{19}NO_3 \cdot HCl$ in the portion of Tablets taken by the formula:

$$0.05C(A_U/A_S),$$

in which C is the concentration, in µg per mL, of USP Hydromorphone Hydrochloride RS in the *Standard preparation*, and A_U and A_S are the absorbances of the solutions from the *Assay preparation* and the *Standard preparation*, respectively.

Hydroquinone



$C_6H_6O_2$ 110.11
1,4-Benzenediol.
Hydroquinone [*123-31-9*].

» Hydroquinone contains not less than 99.0 percent and not more than 100.5 percent of $C_6H_6O_2$, calculated on the anhydrous basis.

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

USP Reference standards ⟨11⟩—*USP Hydroquinone RS.*

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: Prepare a solution of it in methanol containing approximately 1 mg per mL, and prepare a similar solution of USP Hydroquinone RS. Apply 5 µL of each solution to a suitable thin-layer chromatographic plate (see *Chromatography* ⟨621⟩) coated with a 0.25-mm layer of chromatographic silica gel. Allow the spots to dry, and develop the chromatogram in a solvent system consisting of equal volumes of methanol and chloroform 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. Heat on a hot plate or under a lamp until spots appear: the R_f value of the principal spot obtained from the solution under test corresponds to that obtained from the Standard solution.

C: A 1 in 40,000 solution in methanol exhibits an absorbance maximum at 293 ± 2 nm.

Melting range ⟨741⟩: between 172° and 174°.

Water, *Method I* ⟨921⟩: not more than 0.5%.

Residue on ignition ⟨281⟩: not more than 0.5%.

Organic volatile impurities, *Method I* ⟨467⟩: meets the requirements.

Assay—Dissolve about 250 mg of Hydroquinone, accurately weighed, in a mixture of 100 mL of water and 10 mL of 0.1 *N* sulfuric acid, add 3 drops of diphenylamine TS, and titrate with 0.1 *N* ceric sulfate VS until a red-violet endpoint is reached. Perform a blank determination, and make any necessary correction. Each mL of 0.1 *N* ceric sulfate is equivalent to 5.506 mg of $C_6H_6O_2$.

Hydroquinone Cream

» Hydroquinone Cream contains not less than 94.0 percent and not more than 106.0 percent of the labeled amount of $C_6H_6O_2$.

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

USP Reference standards ⟨11⟩—*USP Hydroquinone RS.*

Identification—Dissolve a portion of Cream equivalent to about 50 mg of hydroquinone, in a mixture of equal volumes of methanol and chloroform to make 50 mL: a 5-µL portion of this solution responds to *Identification* test *B* under *Hydroquinone*.

Minimum fill ⟨755⟩: meets the requirements.

Assay—

Standard preparation—Dissolve a suitable quantity of USP Hydroquinone RS in methanol, and dilute quantitatively and stepwise with methanol to obtain a solution having a known concentration of about 10 µg per mL.

Assay preparation—Transfer an accurately weighed portion of Cream, equivalent to about 20 mg of hydroquinone, to a 100-mL beaker. Triturate the Cream with 50 mL of methanol, and filter the liquid through folded filter paper, previously washed with methanol, into a 500-mL volumetric flask. Repeat the trituration and filtration. Dilute, by washing the contents of the filter paper with methanol through the paper into the volumetric flask, to volume, and mix. Pipet 25 mL of this solution into a 100-mL volumetric flask, add methanol to volume, and mix.

Procedure—Concomitantly determine the absorbances of the *Standard preparation* and the *Assay preparation* in 1-cm cells at the wavelength of maximum absorbance at about 293 nm, with a suitable spectrophotometer, using methanol as the blank. Calculate the quantity, in mg, of $C_6H_6O_2$ in each g of the Cream taken by the formula:

$$2(C/W)(A_U/A_S),$$

in which C is the concentration, in mg per mL, of USP Hydroquinone RS in the *Standard preparation*, W is the weight, in g, of Cream taken, and A_U and A_S are the absorbances of the *Assay preparation* and the *Standard preparation*, respectively.

Hydroquinone Topical Solution

» Hydroquinone Topical Solution contains not less than 95.0 percent and not more than 110.0 percent of the labeled amount of $C_6H_6O_2$.

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

USP Reference standards ⟨11⟩—*USP Hydroquinone RS.*

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

pH ⟨791⟩: between 3.0 and 4.2.

Assay—

Mobile phase—Mix 55 volumes of methanol and 45 volumes of water.

Standard preparation—Transfer about 250 mg of USP Hydroquinone RS, accurately weighed, to a 25-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. Transfer 3.0 mL of this solution to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Assay preparation—Transfer an accurately measured volume of Topical Solution, equivalent to about 30 mg of hydroquinone, to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 280-nm detector and a 4-mm × 30-cm column that contains packing L1. The flow rate is about

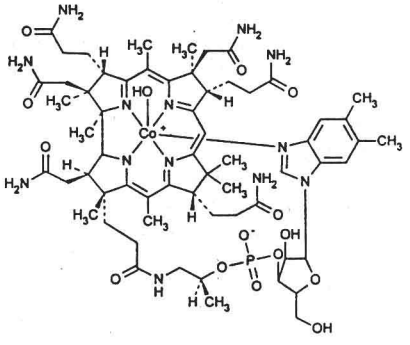
0.8 mL per minute. Chromatograph three replicate injections of the *Standard preparation*, and record the peak responses as directed under *Procedure:* the relative standard deviation is not more than 3.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph by means of a suitable microsyringe or sampling valve, record the chromatograms, and measure the responses for the major peaks. The retention time is about 4 minutes for hydroquinone. Calculate the quantity, in mg, of $C_6H_6O_2$ in each mL of the Topical Solution taken by the formula:

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

in which C is the concentration, in mg per mL, of USP Hydroquinone RS in the *Standard preparation*, V is the volume, in mL, of Topical Solution taken, and r_U and r_S are the peak responses of hydroquinone obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Hydroxocobalamin



$C_{62}H_{89}CoN_{13}O_{15}P$ 1346.36

Cobinamide, dihydroxide, dihydrogen phosphate (ester), mono(inner salt), 3′-ester with 5,6-dimethyl-1-α-D-ribofuranosyl-1*H*-benzimidazole.

Cobinamide dihydroxide dihydrogen phosphate (ester), mono(inner salt), 3′-ester with 5,6-dimethyl-1-α-D-ribofuranosylbenzimidazole [*13422-51-0*].

» Hydroxocobalamin contains not less than 95.0 percent and not more than 102.0 percent of $C_{62}H_{89}CoN_{13}O_{15}P$, calculated on the dried basis.

Packaging and storage—Preserve in tight, light-resistant containers, and store in a cool place.

USP Reference standards ⟨11⟩—*USP Cyanocobalamin RS.*

Identification—

A: The visible absorption spectrum of the solution, prepared for measurement of the absorption as directed under *pH-dependent cobalamins*, exhibits maxima at 426 ± 2 nm, 516 ± 2 nm, and 550 ± 2 nm.

B: Fuse a mixture of about 1 mg of Hydroxocobalamin and about 50 mg of potassium pyrosulfate in a porcelain crucible. Cool, break up the mass with a glass rod, add 3 mL of water, and boil until dissolved. Add 1 drop of phenolphthalein TS, and add 2 *N* sodium hydroxide dropwise until a pink color appears. Add 0.5 g of sodium acetate, 0.5 mL of 1 *N* acetic acid, and 0.5 mL of nitroso R salt solution (1 in 100): a red or orange-red color appears immediately. Add 0.5 mL of hydrochloric acid, and boil for 1 minute: the red or orange-red color persists.

pH ⟨791⟩: between 8.0 and 10.0, in a solution (2 in 100).

Loss on drying ⟨731⟩—Dry it at a pressure below 5 mm of mercury at 100° for 2 hours: it loses between 14.0% and 18.0% of its weight.

pH-dependent cobalamins—

pH 4.0 buffer—Dissolve 2.61 g of sodium acetate and 20.5 g of sodium chloride in 5.25 mL of glacial acetic acid and sufficient water to make 1500 mL of solution, and mix.

pH 9.3 buffer—Dissolve 23.8 g of sodium borate and 402 mg of boric acid in sufficient water to make 1500 mL of solution, and mix.

Procedure—[NOTE—Perform the following test in subdued light.] Transfer about 40 mg of Hydroxocobalamin, accurately weighed, to a 25-mL volumetric flask, dissolve in carbon dioxide–free water, dilute with carbon dioxide–free water to volume, and mix. Transfer 1.0-mL portions of this solution to each of two glass-stoppered test tubes. To one of the tubes, designated *B*, add 3.0 mL of *pH 4.0 buffer*, and mix. To the other tube, designated *U*, add 3.0 mL of *pH 9.3 buffer*, and mix. Determine the absorbance of solution *U*, in a 1-cm cell, at the wavelength of maximum absorbance at about 550 nm, with a suitable spectrophotometer, using solution *B* as the blank. Calculate the percentage of pH-dependent cobalamins, as hydroxocobalamin, by the formula:

$$(100{,}000A)/(19.66W),$$

in which A is the absorbance of solution *U*, and W is the weight, in mg, of Hydroxocobalamin taken: the content, calculated on the dried basis, is between 95.0% and 102.0%.

Limit of cyanocobalamin—

Cyanocobalamin tracer reagent, Cresol–carbon tetrachloride solution, Butanol–benzalkonium chloride solution, and *Alumina-resin column*—Prepare as directed under *Cobalamin Radiotracer Assay* ⟨371⟩.

Procedure—Transfer about 50 mg of Hydroxocobalamin, accurately weighed, to a 25-mL volumetric flask, dissolve in water, dilute with water to volume, and mix. Transfer 5.0 mL of this solution to a glass-stoppered, 50-mL centrifuge tube, and add 5.0 mL of *Cyanocobalamin tracer reagent* and 15 mL of *Cresol–carbon tetrachloride solution.* Insert the stopper, shake gently, centrifuge, carefully remove the upper, aqueous layer by aspiration, and discard the aspirated liquid. Add 25 mL of 5 *N* sulfuric acid, insert the stopper, shake gently, centrifuge, and remove and discard the upper, aqueous layer. Repeat the washing with additional 25-mL portions of the 5 *N* sulfuric acid until the acid wash is colorless (six to eight washings), and discard the acid washings. Add *Cresol–carbon tetrachloride solution* as necessary during the acid washings to maintain the volume of this phase at not less than 10 mL. Wash this solution successively with two 10-mL portions of saturated dibasic sodium phosphate solution and one 10-mL portion of water, and discard all of the aqueous washings. Proceed as directed for *Procedure* under *Cobalamin Radiotracer Assay* ⟨371⟩, beginning with "To the washed extract add 30 mL of a mixture of 2 volumes of *Butanol–Benzalkonium Chloride Solution* and 1 volume of carbon tetrachloride."

Calculation—Calculate the cyanocobalamin content, in µg, of the Hydroxocobalamin taken by the formula:

$$R(C_S/C_U)(A_U/A_S),$$

in which R is the quantity, in µg, of cyanocobalamin in the portion of the Standard solution taken, C_S and C_U are the corrected average radioactivity values, expressed in counts per minute per mL, of the Standard solution and test solution, respectively, and A_U and A_S are the absorbances, determined at 361 nm, of the test solution and the Standard solution, respectively: the limit, calculated on the dried basis, is 5.0%.

Assay—

Cyanocobalamin tracer reagent, Cresol–carbon tetrachloride solution, Phosphate-cyanide solution, Butanol–benzalkonium chloride solution, and *Alumina-resin column*—Prepare as directed under *Cobalamin Radiotracer Assay* ⟨371⟩.

Assay preparation—Transfer about 40 mg of Hydroxocobalamin, accurately weighed, to a 2000-mL volumetric flask, dissolve in water, dilute with water to volume, and mix. Transfer 25.0 mL of this solution to a beaker, add 5.0 mL of *Cyanocobalamin tracer reagent*, and proceed as directed for *Assay Preparation* under *Cobalamin Radiotracer Assay* ⟨371⟩, beginning with "Add, while working *under a hood*, 5 mg of sodium nitrite."

Procedure—Proceed as directed for *Procedure* under *Cobalamin Radiotracer Assay* ⟨371⟩. Calculate the quantity, in µg, of $C_{62}H_{89}CoN_{13}O_{15}P$ in the Hydroxocobalamin taken by the formula:

$$(1346.38/1355.39)(R)(C_S/C_U)(A_U/A_S),$$

in which 1346.38 and 1355.39 are the molecular weights of hydroxocobalamin and cyanocobalamin, respectively, R is the quantity, in µg, of cyanocobalamin in the portion of the Standard solution taken, C_S and C_U are the corrected average radioactivity values, expressed in counts per minute per mL, of the Standard solution and test solution, respectively, and A_U and A_S are the absorbances, determined at 361 nm, of the test solution and the Standard solution, respectively.

Hydroxocobalamin Injection

» Hydroxocobalamin Injection is a sterile solution of Hydroxocobalamin in Water for Injection. It contains not less than 95.0 percent and not more than 115.0 percent of the labeled amount of $C_{62}H_{89}CoN_{13}O_{15}P$.

Packaging and storage—Preserve in single-dose or in multiple-dose containers, preferably of Type I glass, protected from light.

USP Reference standards ⟨11⟩—*USP Cyanocobalamin RS. USP Endotoxin RS.*

Identification—Dilute 3.0 mL of Injection to 100 mL with pH 4.0 buffer (prepared by dissolving 2.61 g of sodium acetate and 20.5 g of sodium chloride in 5.25 mL of glacial acetic acid and sufficient water to make 1500 mL of solution): the ultraviolet-visible absorption spectrum of this solution exhibits maxima at 352 ± 1 nm and 528 ± 2 nm. The ratio A_{352}/A_{528} is between 2.7 and 3.3.

Bacterial endotoxins ⟨85⟩—It contains not more than 0.4 USP Endotoxin Unit per µg of hydroxocobalamin.

pH ⟨791⟩: between 3.5 and 5.0.

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

Assay—

pH 9.3 buffer—Dissolve 23.8 g of sodium borate and 402 mg of boric acid in sufficient water to make 1500 mL of solution, and mix.

Standard preparation—Dissolve in *pH 9.3 buffer* a suitable quantity of USP Cyanocobalamin RS, accurately weighed, and dilute quantitatively, and stepwise if necessary, to obtain a solution having a known concentration of about 30 µg per mL.

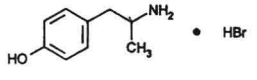
Assay preparation—Transfer an accurately measured volume of Injection, equivalent to about 5 mg of hydroxocobalamin, to a 50-mL volumetric flask containing about 25 mL of *pH 9.3 buffer*. Add 5.0 mL of potassium cyanide solution (1 in 10,000), allow to stand at room temperature for 30 minutes, dilute with *pH 9.3 buffer* to volume, and mix. Transfer 15.0 mL of this solution to a second 50-mL volumetric flask, dilute with *pH 9.3 buffer* to volume, and mix.

Procedure—Concomitantly determine the absorbances of the solutions in 1-cm cells at the wavelength of maximum absorbance at about 361 nm, with a suitable spectrophotometer, using *pH 9.3 buffer* as the blank. Calculate the quantity, in mg, of $C_{62}H_{89}CoN_{13}O_{15}P$ in each mL of the Injection taken by the formula:

$$(1346.38/1355.39)(0.1667C/V)(A_U/A_S),$$

in which 1346.38 and 1355.39 are the molecular weights of hydroxocobalamin and cyanocobalamin, respectively, C is the concentration, in µg per mL, of USP Cyanocobalamin RS in the *Standard preparation*, V is the volume, in mL, of Injection taken, and A_U and A_S are the absorbances of the *Assay preparation* and the *Standard preparation*, respectively.

Hydroxyamphetamine Hydrobromide



$C_9H_{13}NO \cdot HBr$ 232.12

Phenol, 4-(2-aminopropyl)-, hydrobromide.
(±)-*p*-(2-Aminopropyl)phenol hydrobromide [*306-21-8*].

» Hydroxyamphetamine Hydrobromide contains not less than 98.0 percent and not more than 101.5 percent of $C_9H_{13}NO \cdot HBr$, calculated on the dried basis.

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

USP Reference standards ⟨11⟩—*USP Hydroxyamphetamine Hydrobromide RS.*

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: Dissolve about 500 mg of ammonium molybdate in 10 mL of sulfuric acid, and add to this solution about 2 mg of Hydroxyamphetamine Hydrobromide: an intense blue color is produced (*distinction from similar amino compounds such as amphetamine and methamphetamine, which, lacking a phenolic hydroxyl, do not undergo this reaction*).

C: Dissolve about 200 mg in 2 mL of water, and add a solution of 500 mg of potassium carbonate in 2 mL of water. Extract with two 10-mL portions of ether, allow the clear ether solution to evaporate to dryness, and dry at about 80°: the hydroxyamphetamine so obtained melts between 124° and 127° (see *Class I* under *Melting Range or Temperature* ⟨741⟩).

D: To a solution of about 10 mg of it in 10 mL of water add 1 mL of 2 *N* nitric acid, then add silver nitrate TS: a pale yellow precipitate is formed, and it is slightly soluble in 6 *N* ammonium hydroxide.

Melting range ⟨741⟩: between 189° and 192°.

Loss on drying ⟨731⟩—Dry it at 105° for 2 hours: it loses more than 0.5% of its weight.

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

Bromide content—Weigh accurately about 400 mg, and dissolve in 50 mL of water. Add 50 mL of methanol and 10 mL of glacial acetic acid, then add eosin Y TS, and titrate with 0.1 *N* silver nitrate VS. Each mL of 0.1 *N* silver nitrate is equivalent to 7.990 mg of Br: the content of Br, calculated on the dried basis, is between 33.6% and 35.2%.

Ordinary impurities ⟨466⟩—

Test solution: methanol.

Standard solution: methanol.

Eluant: a mixture of toluene, methanol, and ammonium hydroxide (10:4:0.25).

Visualization: 1.

Assay—Dissolve about 400 mg of Hydroxyamphetamine Hydrobromide, accurately weighed, in a mixture of 10 mL of glacial acetic acid and 10 mL of mercuric acetate TS, warming slightly, if necessary, to effect solution. Add crystal violet TS, and titrate with 0.1 *N* perchloric acid VS. Perform a blank determination, and make any necessary correction. Each mL of 0.1 *N* perchloric acid is equivalent to 23.21 mg of $C_9H_{13}NO \cdot HBr$.

Hydroxyamphetamine Hydrobromide Ophthalmic Solution

» Hydroxyamphetamine Hydrobromide Ophthalmic Solution is a sterile, buffered, aqueous solution of Hydroxyamphetamine Hydrobromide. It contains not less than 95.0 percent and not more than 105.0 percent of the labeled amount of $C_9H_{13}NO \cdot HBr$. It contains a suitable antimicrobial agent.

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

USP Reference standards ⟨11⟩—*USP Hydroxyamphetamine Hydrobromide RS.*

Identification—

A: Dissolve about 500 mg of ammonium molybdate in 10 mL of sulfuric acid, and add 0.2 mL of Ophthalmic Solution: an intense blue color is produced (*distinction from similar amino compounds such as amphetamine and methamphetamine, which, lacking a phenolic hydroxyl, do not undergo this reaction*).

B: The dried diacetylhydroxyamphetamine obtained in the *Assay* melts between 96° and 100° (see *Class I* under *Melting Range or Temperature* ⟨741⟩), but the range between beginning and end of melting does not exceed 2.0°.

C: It responds to *Identification* test *D* under *Hydroxyamphetamine Hydrobromide.*

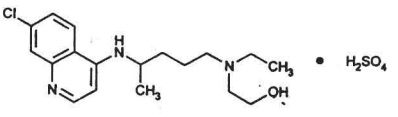
D: Dilute a volume of Ophthalmic Solution, equivalent to about 50 mg of hydroxyamphetamine hydrobromide, with 0.01 *N* hydrochloric acid to 25 mL, and proceed as directed under *Identification—Organic Nitrogenous Bases* ⟨181⟩, using sodium carbonate TS in place of 1 *N* sodium hydroxide, beginning with "Transfer the liquid to a separator": the Ophthalmic Solution meets the requirements of the test.

Sterility—It meets the requirements under *Sterility Tests* ⟨71⟩.

pH ⟨791⟩: between 4.2 and 6.0.

Assay—Transfer an accurately measured volume of Ophthalmic Solution, equivalent to about 100 mg of hydroxyamphetamine hydrobromide, to a 125-mL separator. Wash the solution with 15 mL of chloroform, and discard the washing. Rinse the stopper and the mouth of the separator with a few drops of water. Add 1.05 g of sodium bicarbonate, preventing it from coming in contact with the mouth of the separator, and swirl until most of the bicarbonate has dissolved. By means of a 1-mL syringe, rapidly inject 0.5 mL of acetic anhydride directly into the contents of the separator. Immediately insert the stopper in the separator, and shake vigorously until the evolution of carbon dioxide has ceased (7 to 10 minutes), releasing the pressure as necessary through the stopcock. Allow to stand for 5 minutes, and extract the solution with five 10-mL portions of chloroform, filtering each extract through a pledget of cotton, previously washed with chloroform, into a tared 100-mL beaker. Evaporate the combined chloroform extracts on a steam bath in a current of air or stream of nitrogen to dryness. Dry the residue at 80° for 90 minutes, cool in a desiccator, and weigh. The weight of the diacetylhydroxyamphetamine so obtained, multiplied by 0.9866, represents the weight of $C_9H_{13}NO \cdot HBr$ in the volume of Ophthalmic Solution taken.

Hydroxychloroquine Sulfate



$C_{18}H_{26}ClN_3O \cdot H_2SO_4$ 433.95

Ethanol, 2-[[4-[(7-chloro-4-quinolinyl)amino]pentyl]-ethylamino]-, (±)-, sulfate (1:1) (salt).

(±)-2-[[4-[(7-Chloro-4-quinolyl)amino]pentyl]-ethylamino]ethanol sulfate (1:1) (salt) [*747-36-4*].

» Hydroxychloroquine Sulfate contains not less than 98.0 percent and not more than 102.0 percent of $C_{18}H_{26}ClN_3O \cdot H_2SO_4$, calculated on the dried basis.

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

USP Reference standards ⟨11⟩—*USP Hydroxychloroquine Sulfate RS.*

Identification—

A: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 10 μg per mL.

Medium: dilute hydrochloric acid (1 in 100).

B: *Infrared Absorption* ⟨197K⟩.

C: A solution (1 in 100) responds to the tests for *Sulfate* ⟨191⟩.

Loss on drying ⟨731⟩—Dry it at 105° for 2 hours: it loses not more than 2.0% of its weight.

Ordinary impurities ⟨466⟩—

Test solution: 10% water in methanol.

Standard solution: 10% water in methanol.

Eluant: a mixture of alcohol, water, and ammonium hydroxide (80:16:4).

Visualization: 1.

Organic volatile impurities, *Method I* ⟨467⟩: meets the requirements.

Assay—Dissolve about 100 mg of Hydroxychloroquine Sulfate, accurately weighed, in about 5 mL of water, and dilute quantitatively and stepwise with dilute hydrochloric acid (1 in 100) to obtain a solution containing about 10 μg per mL. Similarly prepare a Standard solution of USP Hydroxychloroquine Sulfate RS. Concomitantly determine the absorbances of both solutions in 1-cm cells at the wavelength of maximum absorbance at about 343 nm, with a suitable spectrophotometer, using dilute hydrochloric acid (1 in 100) as the blank. Calculate the quantity, in mg, of $C_{18}H_{26}ClN_3O \cdot H_2SO_4$ in the portion of Hydroxychloroquine Sulfate taken by the formula:

$$10C(A_U / A_S),$$

in which C is the concentration, in μg per mL, of USP Hydroxychloroquine Sulfate RS in the Standard solution, and A_U and A_S are the absorbances of the solution of Hydroxychloroquine Sulfate and the Standard solution, respectively.

Hydroxychloroquine Sulfate Tablets

» Hydroxychloroquine Sulfate Tablets contain not less than 93.0 percent and not more than 107.0 percent of the labeled amount of $C_{18}H_{26}ClN_3O \cdot H_2SO_4$.

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

USP Reference standards ⟨11⟩—*USP Hydroxychloroquine Sulfate RS.*

Identification—

A: Triturate a quantity of finely powdered Tablets, equivalent to about 1 g of hydroxychloroquine sulfate, with 50 mL of water, and filter: the clear filtrate so obtained responds to *Identification* tests *B* and *C* under *Hydroxychloroquine Sulfate.*

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

Dissolution ⟨711⟩—

Medium: water; 900 mL.

Apparatus 2: 50 rpm.

Time: 60 minutes.

Procedure—Determine the amount of $C_{18}H_{26}ClN_3O \cdot H_2SO_4$ dissolved from ultraviolet absorbances at the wavelength of maximum absorbance at about 343 nm of filtered portions of the solution under test, suitably diluted with *Dissolution Medium,* if necessary, in comparison with a Standard solution having a known concentration of USP Hydroxychloroquine Sulfate RS in the same medium.

Tolerances—Not less than 70% (*Q*) of the labeled amount of $C_{18}H_{26}ClN_3O \cdot H_2SO_4$ is dissolved in 60 minutes.

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

Assay—

Mobile phase—To 800 mL of water, add 100 mL of methanol, 100 mL of acetonitrile, 2.0 mL of phosphoric acid, and 96 mg of sodium 1-pentanesulfonate, mix, and filter. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Solvent mixture—Prepare a mixture of methanol and water (1:1).

Standard preparation—Dissolve an accurately weighed quantity of USP Hydroxychloroquine Sulfate RS in *Solvent mixture,* dilute quantitatively with *Solvent mixture,* and mix to obtain *Solution A* having a known concentration of about 1 mg per mL. Transfer 5.0

mL of this solution to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix to obtain the *Standard preparation* having a known concentration of about 0.05 mg per mL.

Resolution solution—Prepare a solution of chloroquine phosphate in methanol having a concentration of 1 mg per mL. Transfer 5.0 mL of this solution to a 100-mL volumetric flask, add 5.0 mL of *Solution A*, dilute with *Mobile phase* to volume, and mix.

Assay preparation—Weigh and finely powder not less than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 200 mg of hydroxychloroquine sulfate to a 200-mL volumetric flask, add about 150 mL of *Solvent mixture*, and mix. Sonicate, with intermittent shaking, for about 15 minutes, and cool to room temperature. Dilute with *Solvent mixture* to volume, mix, and filter. Transfer 5.0 mL of this solution to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

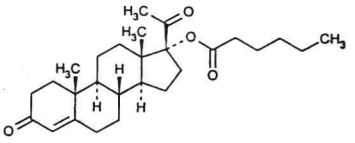
Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 25-cm column that contains 5- to 10-μm packing L1. The flow rate is about 1.0 mL per minute. Chromatograph about 20 μL of the *Resolution solution*, and record the peak responses as directed under *Procedure:* the resolution, R, between chloroquine and hydroxychloroquine is not less than 1.8. Chromatograph replicate injections of the *Standard preparation*, and record the peak responses as directed under *Procedure:* the relative standard deviation is not more than 1.5%.

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 responses for the major peaks. Calculate the quantity, in mg, of hydroxychloroquine sulfate in the portion of Tablets taken by the formula:

$$4000C(r_U/r_S),$$

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

Hydroxyprogesterone Caproate



$C_{27}H_{40}O_4$ 428.60
Pregn-4-ene-3,20-dione, 17-[(1-oxohexyl)oxy]-.
17-Hydroxypregn-4-ene-3,20-dione hexanoate [*630-56-8*].

» Hydroxyprogesterone Caproate contains not less than 97.0 percent and not more than 103.0 percent of $C_{27}H_{40}O_4$, calculated on the anhydrous basis.

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

USP Reference standards ⟨11⟩—*USP Hydroxyprogesterone Caproate RS.*

Identification, *Infrared Absorption* ⟨197K⟩.

Melting range ⟨741⟩: between 120° and 124°.

Specific rotation ⟨781S⟩: between +58° and +64°.
Test solution: 10 mg per mL, in chloroform.

Water, *Method I* ⟨921⟩: not more than 0.1%.

Free *n*-caproic acid—Dissolve 0.20 g in 25 mL of alcohol that previously has been neutralized to a faint pink color following the addition of 2 or 3 drops of phenolphthalein TS. Promptly titrate with 0.020 *N* sodium hydroxide: not more than 0.50 mL of 0.020 *N* sodium hydroxide is required (0.58%).

Ordinary impurities ⟨466⟩—
Test solution: chloroform.
Standard solution: chloroform.
Eluant: a mixture of chloroform and ethyl acetate (3:1).
Visualization: 5; then view under long-wavelength ultraviolet light.

Assay—Transfer about 50 mg of Hydroxyprogesterone Caproate, accurately weighed, to a 100-mL volumetric flask, add alcohol to volume, and mix. Dilute 2.0 mL of this solution with alcohol to volume in a second 100-mL volumetric flask, and mix. Dissolve in alcohol a suitable quantity of USP Hydroxyprogesterone Caproate RS, and dilute quantitatively and stepwise with alcohol to obtain a Standard solution having a known concentration of about 10 μg per mL. Concomitantly determine the absorbances of both solutions in 1-cm cells at the wavelength of maximum absorbance at about 240 nm, using alcohol as the blank. Calculate the quantity, in mg, of $C_{27}H_{40}O_4$ in the Hydroxyprogesterone Caproate taken by the formula:

$$5C(A_U/A_S),$$

in which C is the concentration, in μg per mL, of USP Hydroxyprogesterone Caproate RS in the Standard solution, and A_U and A_S are the absorbances of the solution of Hydroxyprogesterone Caproate and the Standard solution, respectively.

Hydroxyprogesterone Caproate Injection

» Hydroxyprogesterone Caproate Injection is a sterile solution of Hydroxyprogesterone Caproate in a suitable vegetable oil. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{27}H_{40}O_4$.

Packaging and storage—Preserve in single-dose or in multiple-dose containers, preferably of Type I or Type III glass.

USP Reference standards ⟨11⟩—*USP Hydroxyprogesterone Caproate RS.*

Identification—
A: Transfer a volume of Injection, equivalent to 125 mg of hydroxyprogesterone caproate, to a 60-mL separator containing 10 mL of solvent hexane, 8 mL of methanol, and 2 mL of water. Insert the stopper, shake for 2 minutes, and allow the phases to separate. To 3 mL of the lower layer add sulfuric acid dropwise until a color develops, then add 3 mL of methanol: a purple color develops, and the solution, when viewed under long-wavelength ultraviolet light, exhibits a pale yellow fluorescence.

B: Evaporate 4 mL of the *Assay preparation*, obtained as directed in the *Assay*, on a water bath to dryness, and dissolve the residue in 0.5 mL of chloroform. Apply 10 μL of this solution and 10 μL of a solution of USP Hydroxyprogesterone Caproate RS in chloroform, containing 400 μg per mL, to a thin-layer chromatographic plate (see *Chromatography* ⟨621⟩) coated with a 0.25-mm layer of chromatographic silica gel mixture, on a line about 2.5 cm from the bottom edge and about 2 cm apart. Place the plate in a developing chamber that contains and that has been equilibrated with a mixture of 3 volumes of chloroform and 1 volume of ethyl acetate. Develop the plate until the solvent front has moved to about 10 cm above the points of application. Remove the plate, mark the solvent front, and dry. Spray the plate with a mixture of 1 volume of sulfuric acid and 3 volumes of alcohol, and heat in an oven at 105° for 5 minutes: the R_f value of the principal yellowish green spot obtained from the solution under test corresponds to that obtained from the Standard solution.

Water, *Method I* ⟨921⟩: not more than 0.2%.

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

Assay—
Isoniazid reagent—Dissolve 375 mg of isoniazid and 0.47 mL of hydrochloric acid in 500 mL of methanol.

Standard preparation—Dissolve a suitable quantity of USP Hydroxyprogesterone Caproate RS, accurately weighed, in methanol, and dilute quantitatively and stepwise with methanol to obtain a solution having a known concentration of about 50 μg per mL.

Assay preparation—Transfer to a 250-mL volumetric flask an accurately measured volume of Injection, equivalent to about 250 mg of hydroxyprogesterone caproate, add methanol to volume, and mix. Pipet 5 mL of this solution into a 100-mL volumetric flask, add methanol to volume, and mix.

Procedure—Pipet 5 mL of *Assay preparation* into a glass-stoppered, 50-mL conical flask. Pipet 5 mL of *Standard preparation* into a similar flask. To each flask, add 10.0 mL of *Isoniazid reagent*, mix, and allow to stand in a water bath at 30° for about 45 minutes. Concomitantly determine the absorbances of both solutions at the wavelength of maximum absorbance at about 380 nm, with a suitable spectrophotometer, using as a blank a mixture of 5 mL of methanol and 10 mL of *Isoniazid reagent*. Calculate the quantity, in mg, of $C_{27}H_{40}O_4$ in each mL of the Injection taken by the formula:

$$5(C/V)(A_U/A_S),$$

in which C is the concentration, in µg per mL, of USP Hydroxyprogesterone Caproate RS in the *Standard preparation*, V is the volume, in mL, of Injection taken, and A_U and A_S are the absorbances of the solutions from the *Assay preparation* and the *Standard preparation*, respectively.

Hydroxypropyl Cellulose Ocular System

» Hydroxypropyl Cellulose Ocular System contains not less than 85.0 percent and not more than 115.0 percent of the labeled amount of Hydroxypropyl Cellulose. It contains no other substance. It is sterile.

Packaging and storage—Preserve in single-dose containers, at a temperature not exceeding 30°.

USP Reference standards ⟨11⟩—*USP Hydroxypropyl Cellulose RS.*

Identification—Prepare a 1 in 100 solution in methanol, based on the labeled amount of Hydroxypropyl Cellulose. Evaporate 2 drops of the solution on a silver chloride plate so that it forms a thin film: the infrared absorption spectrum of the film so obtained exhibits maxima only at the same wavelengths as that of a similar preparation of USP Hydroxypropyl Cellulose RS.

Sterility—It meets the requirements under *Sterility Tests* ⟨71⟩.

Weight variation—Determine the weight of each of a sufficient number of Systems. Not more than 1 out of 20 varies more than 25% from the average or, failing that, not more than 6 out of 60 (including the original 20) vary more than 25% (but none more than 35%) from the average weight.

Assay—

Standard preparation—Dissolve with agitation an accurately weighed quantity of USP Hydroxypropyl Cellulose RS in water to obtain a solution having a known concentration of about 0.05 mg per mL.

Assay preparation—Transfer a sufficient number of Ocular Systems, to provide about 25 mg of hydroxypropyl cellulose, to a 500-mL volumetric flask, add about 250 mL of water, and dissolve with agitation on a mechanical shaker. Dilute with water to volume, and mix.

Procedure—Separately pipet 2 mL of the *Standard preparation*, the *Assay preparation*, and water, to provide a blank, into individual 50-mL centrifuge tubes. Add to each tube 6.0 mL of a 1 in 2000 solution of anthrone in sulfuric acid, and mix on a vortex mixer. After 40 minutes, again mix, and concomitantly determine the absorbances of the solutions obtained from the *Standard preparation* and the *Assay preparation* at 620 nm, with a suitable spectrophotometer, against the solution from the blank. Calculate the quantity, in mg, of hydroxypropyl cellulose in each Ocular System taken by the formula:

$$(500)(C/N)(A_U/A_S),$$

in which C is the concentration, in mg per mL, of USP Hydroxypropyl Cellulose RS in the *Standard preparation*, N is the number of Ocular Systems taken for the *Assay*, and A_U and A_S are the absorbances of the solutions from the *Assay preparation* and the *Standard preparation*, respectively.

Hydroxypropyl Methylcellulose

Cellulose, 2-hydroxypropyl methyl ether.
Cellulose hydroxypropyl methyl ether [*9004-65-3*].

» Hydroxypropyl Methylcellulose is a propylene glycol ether of methylcellulose. When dried at 105° for 2 hours, it contains methoxy ($-OCH_3$) and hydroxypropoxy ($-OCH_2CHOHCH_3$) groups conforming to the limits for the types of Hydroxypropyl Methylcellulose set forth in the accompanying table.

Substitution Type	Methoxy (percent)		Hydroxypropoxy (percent)	
	Min.	Max.	Min.	Max.
1828	16.5	20.0	23.0	32.0
2208	19.0	24.0	4.0	12.0
2906	27.0	30.0	4.0	7.5
2910	28.0	30.0	7.0	12.0

Packaging and storage—Preserve in well-closed containers.

Labeling—Label it to indicate its substitution type and its viscosity type [viscosity of a solution (1 in 50)].

Identification—

A: Gently add 1 g to the top of 100 mL of water in a beaker, and allow to disperse over the surface, tapping the top of the container to ensure an even dispersion of the substance. Allow the beaker to stand until the substance becomes transparent and mucilaginous (about 5 hours), and swirl the beaker to wet the remaining substance, add a stirring bar, and stir until solution is complete: the mixture remains stable when an equal volume of 1 *N* sodium hydroxide or 1 *N* hydrochloric acid is added.

B: Add 1 g to 100 mL of boiling water, and stir the mixture: a slurry is formed, but the powdered material does not dissolve. Cool the slurry to 20°, and stir: the resulting liquid is a clear or opalescent mucilaginous colloidal mixture.

C: Pour a few mL of the mixture prepared for *Identification* test *B* onto a glass plate, and allow the water to evaporate: a thin, self-sustaining film results.

Apparent viscosity—Place a quantity, accurately weighed and equivalent to 2 g of solids on the dried basis, in a tared, wide-mouth, 250-mL centrifuge bottle, and add 98 g of water previously heated to 80° to 90°. Stir with a propeller-type stirrer for 10 minutes, place the bottle in an ice bath, continue the stirring, and allow to remain in the ice bath for 40 minutes to ensure that hydration and solution are complete. Adjust the weight of the solution to 100 g, if necessary, and centrifuge the solution to expel any entrapped air. Adjust the temperature of the solution to 20 ± 0.1°, and determine the viscosity in a suitable viscosimeter of the Ubbelohde type as directed for *Procedure for Cellulose Derivatives* under *Viscosity* ⟨911⟩. Its viscosity is not less than 80.0% and not more than 120.0% of that stated on the label for viscosity types of 100 centipoises or less, and not less than 75.0% and not more than 140.0% of that stated on the label for viscosity types higher than 100 centipoises.

Loss on drying ⟨731⟩—Dry it at 105° for 2 hours: it loses not more than 5.0% of its weight.

Residue on ignition ⟨281⟩: not more than 1.5% for Hydroxypropyl Methylcellulose having a labeled viscosity of greater than 50 centipoises, not more than 3% for Hydroxypropyl Methylcellulose having a labeled viscosity of 50 centipoises or less, and not more than 5% for Hydroxypropyl Methylcellulose 1828 of all labeled viscosities.

Heavy metals, *Method II* ⟨231⟩: 0.001%, 1 mL of hydroxylamine hydrochloride solution (1 in 5) being added to the solution of the residue.

Organic volatile impurities, *Method IV* ⟨467⟩: meets the requirements.

Assay—[*Caution—Hydriodic acid and its reaction byproducts are highly toxic. Perform all steps of the Assay preparation and the Standard preparation in a properly functioning hood. Specific safety practices to be followed are to be identified to the analyst performing this test.*]

Hydriodic acid—Use a reagent having a specific gravity of at least 1.69, equivalent to 55% HI.

Internal standard solution—Transfer about 2.5 g of toluene, accurately weighed, to a 100-mL volumetric flask containing 10 mL of *o*-xylene, dilute with *o*-xylene to volume, and mix.

Standard preparation—Into a suitable serum vial weigh about 135 mg of adipic acid and 4.0 mL of *Hydriodic acid*, pipet 4 mL of *Internal standard solution* into the vial, and close the vial securely with a suitable septum stopper. Weigh the vial and contents accurately, add 30 µL of isopropyl iodide through the septum with a syringe, again weigh, and calculate the weight of isopropyl iodide added, by difference. Add 90 µL of methyl iodide similarly, again weigh, and calculate the weight of methyl iodide added, by difference. Shake, and allow the layers to separate.

Assay preparation—Transfer about 0.065 g of dried Hydroxypropyl Methylcellulose, accurately weighed, to a 5-mL thick-walled reaction vial equipped with a pressure-tight septum-type closure, add an amount of adipic acid equal to the weight of the test specimen, and pipet 2 mL of *Internal standard solution* into the vial. Cautiously pipet 2 mL of *Hydriodic acid* into the mixture, immediately cap the vial tightly, and weigh accurately. Mix the contents of the vial continuously while heating at 150°, for 60 minutes. Allow the vial to cool for about 45 minutes, and again weigh. If the weight loss is greater than 10 mg, discard the mixture, and prepare another *Assay preparation*.

Chromatographic system—Use a gas chromatograph equipped with a thermal conductivity detector. Under typical conditions, the instrument contains a 1.8-m × 4-mm glass column packed with 20% liquid phase G28 on 100- to 120-mesh support S1C that is not silanized, the column is maintained at 130°, and helium is used as the carrier gas. In a suitable system, the resolution, *R* (see *Chromatography* ⟨621⟩), between the toluene and isopropyl iodide peaks is not less than 2.0.

Calibration—Inject about 2 µL of the upper layer of the *Standard preparation* into the gas chromatograph, and record the chromatogram. Under the conditions described above, the relative retention times of methyl iodide, isopropyl iodide, toluene, and *o*-xylene are approximately 1.0, 2.2, 3.6, and 8.0, respectively. Calculate the relative response factor, F_{mi}, of equal weights of toluene and methyl iodide taken by the formula:

$$Q_{smi}/A_{smi},$$

in which Q_{smi} is the quantity ratio of methyl iodide to toluene in the *Standard preparation*, and A_{smi} is the peak area ratio of methyl iodide to toluene obtained from the *Standard preparation*. Similarly, calculate the relative response factor, F_{ii}, of equal weights of toluene and isopropyl iodide taken by the formula:

$$Q_{sii}/A_{sii},$$

in which Q_{sii} is the quantity ratio of isopropyl iodide to toluene in the *Standard preparation*, and A_{sii} is the peak area ratio of isopropyl iodide to toluene obtained from the *Standard preparation*.

Procedure—Inject about 2 µL of the upper layer of the *Assay preparation* into the gas chromatograph, and record the chromatogram. Calculate the percentage of methoxy in the Hydroxypropyl Methylcellulose taken by the formula:

$$2(31/142)F_{mi}A_{umi}(W_t/W_u),$$

in which 31/142 is the ratio of the formula weights of methoxy and methyl iodide, F_{mi} is defined under *Calibration*, A_{umi} is the ratio of the area of the methyl iodide peak to that of the toluene peak obtained from the *Assay preparation*, W_t is the weight, in g, of toluene in the *Internal standard solution*, and W_u is the weight, in g, of Hydroxypropyl Methylcellulose taken for the *Assay*. Similarly, calculate the percentage of hydroxypropoxy in the Hydroxypropyl Methylcellulose taken by the formula:

$$2(75/170)F_{ii}A_{uii}(W_t/W_u),$$

in which 75/170 is the ratio of the formula weights of hydroxypropoxy and isopropyl iodide, F_{ii} is defined under *Calibration*, A_{uii} is the ratio of the area of the isopropyl iodide peak to that of the toluene peak obtained from the *Assay preparation*, W_t is the weight, in g, of toluene in the *Internal standard solution*, and W_u is the weight, in g, of Hydroxypropyl Methylcellulose taken for the *Assay*.

Hydroxypropyl Methylcellulose Ophthalmic Solution

» Hydroxypropyl Methylcellulose Ophthalmic Solution is a sterile solution of Hydroxypropyl Methylcellulose. It contains not less than 85.0 percent and not more than 115.0 percent of the labeled amount of Hydroxypropyl Methylcellulose. It may contain suitable antimicrobial, buffering, and stabilizing agents.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—*USP Hydroxypropyl Methylcellulose RS.*

Identification—

A: It responds to *Identification* test *C* under *Hydroxypropyl Methylcellulose*.

B: Heat 5 mL of Ophthalmic Solution in a test tube over a low flame: the warm solution turns cloudy but clears upon chilling.

Sterility—It meets the requirements under *Sterility Tests* ⟨71⟩.

pH ⟨791⟩: between 6.0 and 7.8.

Assay—

Standard preparation—Dissolve a suitable quantity of USP Hydroxypropyl Methylcellulose RS, accurately weighed, in water, and dilute quantitatively with water to obtain a solution having a known concentration of about 100 µg per mL.

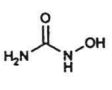
Assay preparation—Dilute quantitatively an accurately measured volume of Ophthalmic Solution with water to obtain a solution having an equivalent concentration of approximately 100 µg of hydroxypropyl methylcellulose per mL.

Procedure—Pipet 2 mL each of the *Standard preparation*, the *Assay preparation*, and water to provide a blank, into separate, glass-stoppered test tubes. To each tube add 5.0 mL of diphenylamine solution (prepared by dissolving 3.75 g of colorless diphenylamine crystals in 150 mL of glacial acetic acid and diluting the solution with 90 mL of hydrochloric acid), mix, and immediately insert the tubes into an oil bath at 105° to 110° for 30 minutes, the temperature being kept uniform within 0.1° during heating. Remove the tubes, and place them in an ice-water bath for 10 minutes or until thoroughly cool. Concomitantly determine, at room temperature, the absorbances of the solutions from the *Standard preparation* and the *Assay preparation* at 635 nm, with a suitable spectrophotometer, using the water solution as the blank. Calculate the quantity, in mg, of hydroxypropyl methylcellulose in each mL of the Ophthalmic Solution taken by the formula:

$$0.001C(d/V)(A_U/A_S),$$

in which C is the concentration, in µg per mL, of USP Hydroxypropyl Methylcellulose RS in the Standard solution, d is the dilution fold of V used to obtain the *Assay preparation*, V is the volume, in mL, of Ophthalmic Solution taken, and A_U and A_S are the absorbances of the solutions from the *Assay preparation* and the *Standard preparation*, respectively.

Hydroxyurea



$CH_4N_2O_2$ 76.05

Urea, hydroxy-.
Hydroxyurea [*127-07-1*].

» Hydroxyurea contains not less than 97.0 percent and not more than 103.0 percent of $CH_4N_2O_2$, calculated on the dried basis.

Packaging and storage—Preserve in tight containers, in a dry atmosphere.

USP Reference standards ⟨11⟩—*USP Hydroxyurea RS.*

Identification, *Infrared Absorption* ⟨197K⟩.

Loss on drying ⟨731⟩—Dry it in vacuum at 60° for 3 hours: it loses not more than 1.0% of its weight.

Residue on ignition ⟨281⟩: not more than 0.50%.

Heavy metals ⟨231⟩: not more than 0.003%.

Urea and related compounds—

Developing solvent—Shake equal volumes of isobutyl alcohol and water in a separator and allow the layers to separate. Use the upper layer as the *Mobile phase* and the lower layer as the *Stationary phase.*

p-Dimethylaminobenzaldehyde solution, 1%—Dissolve 1.0 g of *p*-dimethylaminobenzaldehyde in 50 mL of alcohol, add 2 mL of hydrochloric acid, and dilute with alcohol to 100.0 mL.

pH 6.5 buffer solution—Mix 700 mL of 0.2 *M* dibasic sodium phosphate and 300 mL of 0.1 *M* citric acid.

Standard preparation—Prepare a solution of urea in water, containing 0.1 mg per mL.

Test preparation—Dissolve 10.0 mg of Hydroxyurea in 1.0 mL of water.

Procedure—Treat a suitable chromatographic paper strip (Whatman No. 1 or equivalent) by dipping it in *pH 6.5 buffer solution.* Dry the paper strip, and apply 100 µL of the *Test preparation* and 50 µL of the *Standard preparation.* Place the strip in a chromatographic chamber for descending chromatography containing the *Stationary phase* in the bottom of the chamber and the *Mobile phase* in the trough. Develop for 24 hours, remove the strip from the chamber, air-dry, and develop again for 24 hours. Remove the strip, air-dry, spray with *p-Dimethylaminobenzaldehyde solution, 1%,* and heat at 90° for 1 to 2 minutes. Not more than two spots, other than the major component, are present in the *Test preparation,* and their intensities are not greater than the intensity of the spot from the *Standard preparation* (0.5% of each impurity). The R_f values relative to hydroxyurea, the principal spot, are 0.65 and 1.26 (urea).

Organic volatile impurities, *Method I* ⟨467⟩: meets the requirements.

Assay—

Mobile phase—Use degassed water.

Internal standard solution—Dissolve uracil in water to obtain a solution having a concentration of about 0.12 mg per mL.

Standard preparation—Transfer about 50 mg of USP Hydroxyurea RS, accurately weighed, to a 50-mL volumetric flask, add 10 mL of *Internal standard solution,* dilute with water to volume, and mix.

Resolution solution—Dissolve suitable quantities of USP Hydroxyurea RS and hydroxylamine hydrochloride in water to obtain a solution containing about 1 mg and 4 mg per mL, respectively.

Assay preparation—Transfer about 50 mg of Hydroxyurea, accurately weighed, to a 50-mL volumetric flask, add 10 mL of *Internal standard solution,* dilute with water to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 214-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L1. The flow rate is about 0.5 mL per minute. Chromatograph the *Resolution solution,* and record the peak responses as directed under *Procedure:* the resolution, *R,* between the hydroxylamine and hydroxyurea peaks is not less than 1.0. Chromatograph the *Standard preparation,* and record the peak responses as directed under *Procedure:* the relative standard deviation for replicate injections is not more than 2.0%.

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 responses for the major peaks. The relative retention times are about 0.5 for hydroxyurea and 1.0 for uracil. Calculate the quantity, in mg, of $CH_4N_2O_2$ in the portion of Hydroxyurea taken by the formula:

$$50C(R_U/R_S),$$

in which C is the concentration, in mg per mL, of USP Hydroxyurea RS in the *Standard preparation,* and R_U and R_S are the response ratios of the hydroxyurea peak to the internal standard peak obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Hydroxyurea Capsules

» Hydroxyurea Capsules contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $CH_4N_2O_2$.

Packaging and storage—Preserve in tight containers, in a dry atmosphere.

USP Reference standards ⟨11⟩—*USP Hydroxyurea RS.*

Identification—Transfer a portion of the Capsule contents, equivalent to about 30 mg of hydroxyurea, to a suitable centrifuge tube, and add 10 mL of anhydrous methanol. Mix, and centrifuge for 3 minutes. Transfer 1.0 mL of the clear supernatant liquid to a mortar containing 500 mg of potassium bromide, triturate to a homogeneous blend, dry in a vacuum desiccator at 60° for 3 hours, and prepare a suitable disk: the infrared absorption spectrum exhibits maxima only at the same wavelengths as that of a similar preparation of USP Hydroxyurea RS.

Dissolution ⟨711⟩—

Medium: water; 500 mL.

Apparatus 2: 50 rpm.

Time: 30 minutes.

Procedure—Determine the amount of $CH_4N_2O_2$ dissolved, employing the procedure set forth in the *Assay,* making any necessary modifications.

Tolerances—Not less than 80% (Q) of the labeled amount of $CH_4N_2O_2$ is dissolved in 30 minutes.

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

Assay—

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

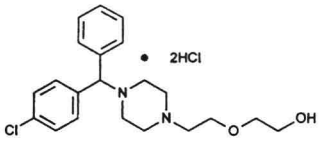
Assay preparation—Remove, as completely as possible, the contents of not less than 20 Capsules, weigh, and place in a glass mortar. Grind to a fine powder, and transfer an accurately weighed portion of the powder, equivalent to about 2000 mg of hydroxyurea, to a 1000-mL volumetric flask. Add about 900 mL of water, sonicate for 5 minutes, stir with the aid of a magnetic stirrer for 30 minutes, dilute with water to volume, mix, and sonicate for an additional 5 minutes. Filter a portion of the resulting solution, discarding the first 10 mL of the filtrate. Transfer 25.0 mL of the clear filtrate to a 50-mL volumetric flask, add 10 mL of *Internal standard solution,* dilute with water to volume, and mix.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Hydroxyurea.* Calculate the quantity, in mg, of $CH_4N_2O_2$ in the portion of Capsules taken by the formula:

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

in which C is the concentration, in mg per mL, of USP Hydroxyurea RS in the *Standard preparation,* and R_U and R_S are the response ratios of the hydroxyurea peak to the internal standard peak obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Hydroxyzine Hydrochloride



$C_{21}H_{27}ClN_2O_2 \cdot 2HCl$ 447.83
Ethanol, 2-[2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]-ethoxy]-, dihydrochloride, (±)-.
(±)-2-[2-[4-(*p*-Chloro-α-phenylbenzyl)-1-piperazinyl]ethoxy]ethanol dihydrochloride [*2192-20-3*].

» Hydroxyzine Hydrochloride, contains not less than 98.0 percent and not more than 100.5 percent of $C_{21}H_{27}ClN_2O_2 \cdot 2HCl$, calculated on the dried basis.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—*USP Hydroxyzine Hydrochloride RS. USP p-Chlorobenzhydrylpiperazine RS.*

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 10 μg per mL.

Medium: alcohol. Absorptivities at 230 nm, calculated on the dried basis, do not differ by more than 3.0%.

C: To 10 mL of a solution (1 in 400) add 2 drops of nitric acid and 1 mL of silver nitrate TS: a curdy, white precipitate, insoluble in 2 *N* nitric acid, but soluble in 6 *N* ammonium hydroxide, separates (*presence of chloride*).

Loss on drying ⟨731⟩—Dry it in vacuum at 75° for 3 hours: it loses not more than 5.0% of its weight.

Residue on ignition ⟨281⟩: not more than 0.5%.

Heavy metals, *Method II* ⟨231⟩: 0.002%.

Chromatographic purity—

Mobile phase—Prepare a filtered and degassed mixture of acetonitrile and 0.12 *N* sulfuric acid (90:10). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve an accurately weighed quantity of USP Hydroxyzine Hydrochloride RS quantitatively in *Mobile phase* to obtain a solution having a known concentration of about 1.8 μg per mL.

Resolution solution—Dissolve suitable quantities of USP Hydroxyzine Hydrochloride RS and USP *p*-Chlorobenzhydrylpiperazine RS in *Mobile phase* to obtain a solution containing 3.6 μg of each per mL.

Test preparation—Transfer an accurately weighed quantity of Hydroxyzine Hydrochloride to a suitable volumetric flask, dissolve in and dilute with *Mobile phase* to volume to obtain a solution containing a known concentration of about 0.6 mg of specimen per mL, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 230-nm detector, and two series-coupled 3-mm × 10-cm columns that contain packing L3. The flow rate is about 0.4 mL per minute. Chromatograph the *Resolution solution* and the *Standard preparation*, and record the peak responses as directed under *Procedure:* the resolution, *R*, between the *p*-chlorobenzhydrylpiperazine and hydroxyzine peaks is not less than 1.2, and the relative standard deviation for replicate injections of the *Standard preparation* is not more than 2.0%.

Procedure—Separately inject equal volumes (about 20 μL) of the *Standard preparation* and the *Test preparation* into the chromatograph, record the chromatograms for a total time of not less than 1.8 times the retention time of the hydroxyzine peak, and measure the response for each peak, except for the main hydroxyzine peak in the chromatogram obtained from the *Test preparation*. Calculate the apparent percentage of each impurity in the specimen taken by the formula:

$$0.1(C_S / C_U)(r_U / r_S),$$

in which C_S is the concentration, in μg per mL, of USP Hydroxyzine Hydrochloride RS in the *Standard preparation*, C_U is the concentration, in mg per mL, of specimen in the *Test preparation*, r_U is the peak response of a given impurity in the chromatogram obtained from the *Test preparation*, and r_S is the peak response of hydroxyzine in the chromatogram obtained from the *Standard preparation:* not more than 0.3% of any impurity is found, and the sum of all impurities found is not greater than 1.5%.

Organic volatile impurities, *Method I* ⟨467⟩: meets the requirements.

Assay—Dissolve about 80 mg of Hydroxyzine Hydrochloride, accurately weighed, in 50 mL of a mixture of acetic anhydride and glacial acetic acid (7:3), and titrate with 0.1 *N* perchloric acid VS, determining the endpoint potentiometrically, using a glass electrode and a silver–silver chloride electrode containing saturated lithium perchlorate and saturated silver 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 22.39 mg of $C_{21}H_{27}ClN_2O_2 \cdot 2HCl$.

Hydroxyzine Hydrochloride Injection

» Hydroxyzine Hydrochloride Injection is a sterile solution of Hydroxyzine Hydrochloride in Water for Injection. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{21}H_{27}ClN_2O_2 \cdot 2HCl$.

Packaging and storage—Preserve in single-dose or in multiple-dose containers, protected from light.

USP Reference standards ⟨11⟩—*USP Hydroxyzine Hydrochloride RS. USP Endotoxin RS.*

Identification—Dilute a volume of Injection with 0.1 *N* hydrochloric acid to obtain a solution having a concentration of about 20 μg of hydroxyzine hydrochloride per mL: the ultraviolet absorption spectrum of this solution exhibits maxima and minima at the same wavelengths as that of a 1 in 50,000 solution of USP Hydroxyzine Hydrochloride RS in 0.1 *N* hydrochloric acid, concomitantly measured.

Bacterial endotoxins ⟨85⟩—It contains not more than 3.6 USP Endotoxin Units per mg of hydroxyzine hydrochloride.

pH ⟨791⟩: between 3.5 and 6.0.

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

Assay and limit of 4-chlorobenzophenone—

Mobile phase—Adjust about 1000 mL of *Buffer No. 1* (see *Phosphate Buffers and Other Solutions* in the section, *Media and Diluents*, under *Antibiotics—Microbial Assays* ⟨81⟩) with 10 *N* potassium hydroxide to a pH of 6.6. To about 35 volumes of this solution add about 65 volumes of methanol, mix, and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve accurately weighed quantities of USP Hydroxyzine Hydrochloride RS and 4-chlorobenzophenone in *Mobile phase*, and dilute quantitatively with *Mobile phase* to obtain a solution having known concentrations of about 250 μg of USP Hydroxyzine Hydrochloride RS and 0.5 μg of 4-chlorobenzophenone per mL. Protect this solution from light.

Assay preparation—Transfer an accurately measured volume of Injection, equivalent to about 125 mg of hydroxyzine hydrochloride, to a 50-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. Pipet 10 mL of this solution into a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. Protect this solution from light.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4-mm × 30-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 under *Procedure:* the tailing factors for the 4-chlorobenzophenone and hydroxyzine peaks are not more than 2.5, the resolution, *R*, between the 4-chlorobenzophenone and hydroxyzine peaks is not less than 2.0, and the relative

standard deviation for replicate injections of the *Standard preparation* is not more than 2.0%. The relative retention times are about 0.75 for 4-chlorobenzophenone and 1.0 for hydroxyzine.

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 responses for the major peaks. Calculate the quantity, in mg, of hydroxyzine hydrochloride ($C_{21}H_{27}ClN_2O_2 \cdot HCl$) in each mL of the Injection taken by the formula:

$$0.5(C/V)(r_U/r_S),$$

in which C is the concentration, in µg per mL, of USP Hydroxyzine Hydrochloride RS in the *Standard preparation*, V is the volume, in mL, of Injection taken, and r_U and r_S are the hydroxyzine peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively. The ratio of the response of the 4-chlorobenzophenone peak to that of the hydroxyzine peak obtained from the *Assay preparation* does not exceed the corresponding ratio of peak responses obtained from the *Standard preparation* (0.2%).

Hydroxyzine Hydrochloride Syrup

» Hydroxyzine Hydrochloride Syrup contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{21}H_{27}ClN_2O_2 \cdot 2HCl$.

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

USP Reference standards ⟨11⟩—*USP Hydroxyzine Hydrochloride RS.*

Identification—Dilute a volume of Syrup, equivalent to about 20 mg of hydroxyzine hydrochloride, with 50 mL of methanol, and mix. Apply 100 µL of this solution and 100 µL of a solution in the same medium containing about 350 µg of USP Hydroxyzine Hydrochloride RS per mL to a suitable thin-layer chromatographic plate (see *Chromatography* ⟨621⟩), coated with a 0.25-mm layer of chromatographic silica gel and dried in air for 30 minutes followed by drying in vacuum at 140° for 30 minutes. Allow the spots to dry, and develop the chromatogram in a solvent system consisting of a mixture of toluene, alcohol, and ammonium hydroxide (150:95:1) 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. Locate the spots by lightly spraying with potassium iodoplatinate TS: the R_f value of the principal spot obtained from the test solution corresponds to that obtained from the Standard solution.

Assay—

Mobile phase and *Chromatographic system*—Proceed as directed in the *Assay* under *Hydroxyzine Hydrochloride Tablets.*

Standard preparation—Dissolve a suitable quantity of USP Hydroxyzine Hydrochloride RS, accurately weighed, in water to obtain a solution having a known concentration of about 100 µg per mL.

Assay preparation—Transfer an accurately measured volume of Syrup, equivalent to about 20 mg of hydroxyzine hydrochloride, to a 200-mL volumetric flask, dilute with water to volume, mix, and filter a portion through a polytef membrane filter (5-µm or finer porosity).

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Hydroxyzine Hydrochloride Tablets.* Calculate the quantity, in mg, of $C_{21}H_{27}ClN_2O_2 \cdot 2HCl$ in each mL of the Syrup taken by the formula:

$$0.2(C/V)(r_U/r_S),$$

in which C is the concentration, in µg per mL, of USP Hydroxyzine Hydrochloride RS in the *Standard preparation*, V is the volume, in mL, of Syrup taken, and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Hydroxyzine Hydrochloride Tablets

» Hydroxyzine Hydrochloride Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{21}H_{27}ClN_2O_2 \cdot 2HCl$.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—*USP Hydroxyzine Hydrochloride RS.*

Identification—Triturate a quantity of finely powdered Tablets, equivalent to about 100 mg of hydroxyzine hydrochloride, with 50 mL of methanol, and filter. Apply 100 µL of this solution and 100 µL of a solution, in the same medium containing 2 mg of USP Hydroxyzine Hydrochloride RS per mL to a suitable thin-layer chromatographic plate (see *Chromatography* ⟨621⟩) coated with a 0.25-mm layer of chromatographic silica gel and dried in air for 30 minutes followed by drying in vacuum at 140° for 30 minutes. Proceed as directed in the *Identification* test under *Hydroxyzine Hydrochloride Syrup*, beginning with "Allow the spots to dry."

Dissolution ⟨711⟩—

Medium: water; 800 mL.

Apparatus—Proceed as directed for *Uncoated Tablets* under *Disintegration* ⟨701⟩, beginning with "Place 1 Tablet in each of the six tubes of the basket," with these exceptions: (a) the disks are not used; (b) the apparatus is adjusted so that the bottom of the basket-rack assembly descends to 1.0 ± 0.1 cm from the inside bottom surface of the vessel on the downward stroke; (c) the 10-mesh, stainless-steel cloth in the basket-rack assembly is replaced with 40-mesh, stainless-steel cloth; and (d) 40-mesh, stainless-steel cloth is fitted to the top of the basket-rack assembly if necessary to prevent any dosage unit from floating out of the tubes of the assembly.

Time: 45 minutes.

Procedure—Determine the amount of $C_{21}H_{27}ClN_2O_2 \cdot 2HCl$ dissolved from ultraviolet absorbances at the wavelength of maximum absorbance at about 230 nm of filtered portions of the solution under test, suitably diluted with water, if necessary, in comparison with a Standard solution having a known concentration of USP Hydroxyzine Hydrochloride RS in the same medium. Calculate the amount of $C_{21}H_{27}ClN_2O_2 \cdot 2HCl$ dissolved per Tablet.

Tolerances—Not less than 75% of the labeled amount of $C_{21}H_{27}ClN_2O_2 \cdot 2HCl$ is dissolved in 45 minutes.

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

Assay—

Mobile phase—Dissolve 6.8 g of monobasic potassium phosphate in 1000 mL of water, add 1000 mL of methanol, and mix. Filter the solution through a polytef membrane filter (5 µm or finer porosity), and degas.

Standard preparation—Dissolve a suitable quantity of USP Hydroxyzine Hydrochloride RS, accurately weighed, in methanol to obtain a solution having a known concentration of about 100 µg per mL.

Assay preparation—Place 20 Tablets in a high-speed blender jar containing 400.0 mL of methanol, and blend for 5 minutes. The Tablets are completely disintegrated. Allow to settle, and filter a portion of the supernatant liquid through a polytef membrane filter (1 µm or finer porosity). Dilute an accurately measured volume of the filtrate so obtained quantitatively with methanol to obtain an *Assay preparation* having a concentration of about 100 µg of hydroxyzine hydrochloride per mL.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 232-nm detector and a 4.6-mm × 25-cm column that contains packing L9. The flow rate is about 2.0 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed under *Procedure:* the relative standard deviation is not more than 2.5%.

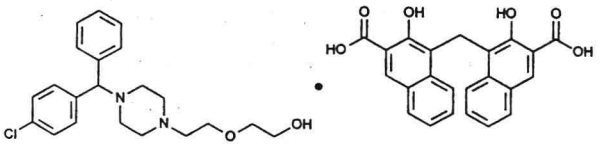
Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of $C_{21}H_{27}ClN_2O_2 \cdot 2HCl$ in each Tablet taken by the formula:

$$(L/D)(C)(r_U/r_S),$$

in which L is the labeled quantity, in mg, of hydroxyzine hydrochloride in each Tablet, D is the concentration, in µg per mL, of

hydroxyzine hydrochloride in the *Assay preparation* on the basis of the labeled quantity in each Tablet and the extent of dilution, C is the concentration in µg per mL, of USP Hydroxyzine 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.

Hydroxyzine Pamoate



$C_{21}H_{27}ClN_2O_2 \cdot C_{23}H_{16}O_6$ 763.27

Ethanol, 2-[2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]-ethoxy]-, (±)-, compd. with 4,4′-methylenebis[3-hydroxy-2-naphthalenecarboxylic acid] (1:1).

(±)-2-[2-[4-(*p*-Chloro-α-phenylbenzyl)-1-piperazinyl]ethoxy]ethanol 4,4′-methylenebis[3-hydroxy-2-naphthoate] (1:1) [*10246-75-0*].

» Hydroxyzine Pamoate contains not less than 97.0 percent and not more than 102.0 percent of $C_{21}H_{27}ClN_2O_2 \cdot C_{23}H_{16}O_6$, calculated on the anhydrous basis.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—*USP Hydroxyzine Pamoate RS. USP Hydroxyzine Hydrochloride RS. USP Pamoic Acid RS.*

Identification—

A: Transfer about 85 mg (equivalent to about 50 mg of hydroxyzine hydrochloride) to a separator containing 25 mL of 1 *N* sodium hydroxide, and extract with three 20-mL portions of chloroform. Evaporate the combined chloroform extracts on a steam bath with the aid of a current of air to dryness, and dissolve the residue in 0.1 *N* hydrochloric acid to make 100 mL. Dilute a 1-mL portion of this solution with 0.1 *N* hydrochloric acid to 50 mL: the ultraviolet absorption spectrum of the solution so obtained exhibits maxima and minima at the same wavelengths as that of a 1 in 100,000 solution of USP Hydroxyzine Hydrochloride RS in 0.1 *N* hydrochloric acid, concomitantly measured.

B: Prepare a solution of it in a mixture of equal volumes of 0.1 *N* sodium hydroxide and acetone containing 2 mg per mL. Apply 10 µL of this solution and 10 µL of a solution of USP Hydroxyzine Pamoate RS in the same medium, having a concentration of 2 mg per mL to a suitable thin-layer chromatographic plate (see *Chromatography* ⟨621⟩) coated with a 0.50-mm layer of chromatographic silica gel. Allow the spots to dry, and develop the chromatogram in 0.1 *N* hydrochloric acid 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 locate the spots on the plate by viewing under long-wavelength ultraviolet light: the R_f value of the principal spot, representing the pamoate moiety, obtained from the test solution corresponds to that obtained from the Standard solution. Spray the plate lightly with potassium iodoplatinate TS: the R_f value of the principal spot, representing the hydroxyzine moiety, obtained from the test solution corresponds to that obtained from the Standard solution.

Water, *Method I* ⟨921⟩: not more than 5.0%.

Residue on ignition ⟨281⟩: not more than 0.5%.

Heavy metals, *Method II* ⟨231⟩: 0.005%.

Organic volatile impurities, *Method V* ⟨467⟩: meets the requirements.

Solvent—Use dimethyl sulfoxide as the solvent.

Pamoic acid content—Dissolve an accurately weighed quantity of USP Pamoic Acid RS in dimethylformamide to obtain a solution having a known concentration of about 0.45 mg per mL. Transfer 2.0 mL of the resulting solution to a 50-mL volumetric flask, dilute with *Mobile phase*, prepared as directed in the *Assay*, to volume, and mix. Filter through a membrane filter of 0.5 µm or finer porosity to obtain the *Standard preparation*. Chromatograph this *Standard preparation* as directed in the *Assay*. From the chromatogram of the *Assay preparation* obtained in the *Assay*, calculate the quantity, in mg, of pamoic acid ($C_{23}H_{16}O_6$) in the portion of Hydroxyzine Pamoate taken by the formula:

$$2500C(r_U/r_S),$$

in which C is the concentration, in mg per mL, of USP Pamoic Acid RS in the *Standard preparation*, and r_U and r_S are the pamoic acid peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively: the content of pamoic acid is between 49.4% and 51.9%, calculated on the anhydrous basis.

Assay—

Mobile phase—Dissolve 8.65 g of sodium 1-octanesulfonate in about 1000 mL of water in a 2000-mL volumetric flask, add 4.0 mL of phosphoric acid, dilute with water to volume, mix, and filter through a membrane filter of 0.5 µm or finer porosity. Prepare a suitable mixture of this solution and acetonitrile (45:55), making any adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve an accurately weighed quantity of USP Hydroxyzine Hydrochloride RS in dimethylformamide to obtain a solution having a known concentration of about 1 mg per mL. Transfer 2.0 mL of the resulting solution to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, mix, and filter through a membrane filter of 0.5 µm or finer porosity.

Assay preparation—Transfer about 90 mg of Hydroxyzine Pamoate, accurately weighed, to a 50-mL volumetric flask, dissolve in dimethylformamide, dilute with dimethylformamide to volume, and mix. Transfer 2.0 mL of the resulting solution to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, mix, and filter through a membrane filter of 0.5 µm or finer porosity, discarding the first 5 mL of the filtrate.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 230-nm detector and a 3.9-mm × 30-cm column that contains packing L1. The flow rate is about 1.5 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed under *Procedure:* the column efficiency, calculated from the analyte peak, is not less than 2000 theoretical plates, and the relative standard deviation for replicate injections is not more than 2%. Chromatograph the *Assay preparation*, and record the peak responses as directed under *Procedure:* the resolution, R, between hydroxyzine and pamoic acid is not less than 1.5.

Procedure—Separately inject equal volumes (about 50 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. The relative retention times are about 0.5 for hydroxyzine and 1.0 for pamoic acid. Calculate the quantity, in mg, of $C_{21}H_{27}ClN_2O_2 \cdot C_{23}H_{16}O_6$ in the portion of Hydroxyzine Pamoate taken by the formula:

$$2500(763.29/447.83)C(r_U/r_S),$$

in which 763.29 and 447.83 are the molecular weights of hydroxyzine pamoate and hydroxyzine hydrochloride, respectively, C is the concentration, in mg per mL, of USP Hydroxyzine Hydrochloride RS in the *Standard preparation*, and r_U and r_S are the hydroxyzine peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Hydroxyzine Pamoate Capsules

» Hydroxyzine Pamoate Capsules contain hydroxyzine pamoate ($C_{21}H_{27}ClN_2O_2 \cdot C_{23}H_{16}O_6$) equivalent to not less than 90.0 percent and not more than 110.0 percent of the labeled amount of hydroxyzine hydrochloride ($C_{21}H_{27}ClN_2O_2 \cdot 2HCl$).

Packaging and storage—Preserve in well-closed containers.