1,4-Pentanediamine, N^4-(7-chloro-4-quinolinyl)-N^1,N^1-diethyl-.
7-Chloro-4-[[4-(diethylamino)-1-methylbutyl]amino]quinoline [54-05-7].

» Chloroquine contains not less than 98.0 percent and not more than 102.0 per cent of $C_{18}H_{26}ClN_3$, calculated on the dried basis.

Packaging and storage—Preserve in well-closed containers. Store at 25°, excursions permitted between 15 ° and 30°.

USP Reference standards ⟨11⟩**—**
USP Chloroquine Phosphate RS

Identification—

A: Dissolve 35 mg in 4 mL of chloroform, and pass through a dry filter: the IR absorption spectrum of the solution so obtained exhibits maxima only at the same wavelengths as that of a solution of USP Chloroquine Phosphate RS prepared as directed in *Identification* test *A* under *Chloroquine Phosphate.*

B: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 10 µg per mL.

Medium: dilute hydrochloric acid (1 in 1000).

Ratio: A_{343} / A_{329}, between 1.00 and 1.15.

Melting range ⟨741⟩**:** between 87° and 92°.

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

Residue on ignition ⟨281⟩**:** not more than 0.2%.

Assay—Dissolve about 250 mg of Chloroquine, accurately weighed, in 50 mL of glacial acetic acid, add cr ystal violet TS, and titrate with 0.1 N per chloric acid VS. Per form a blank determination, and make any necessar y correction. Each mL of 0.1 N per chloric acid is equivalent to 15.99 mg of $C_{18}H_{26}ClN_3$.

Chloroquine Hydrochloride Injection

$C_{18}H_{26}ClN_3 \cdot 2HCl$ 392.79
1,4-Pentanediamine, N^4-(7-chloro-4-quinolinyl)-N^1,N^1-diethyl-, dihydrochloride.
7-(Chloro-4-4-diethylamino)-1-methylbutylaminoquinoline dihydrochloride [3545-67-3].

» Chloroquine Hydrochloride Injection is a sterile solution of Chloroquine in W ater for Injection prepared with the aid of Hydrochloric Acid. It contains, in each mL, not less than 47.5 mg and not more than 52.5 mg of $C_{18}H_{26}ClN_3 \cdot 2HCl$.

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

USP Reference standards ⟨11⟩**—**
USP Chloroquine Phosphate RS
USP Endotoxin RS

Identification—

A: The UV absorption spectrum of the solution employed for measurement of absorbance in the *Assay* exhibits maxima and minima at the same wavelengths as that of a similar solution of USP Chloroquine Phosphate RS , concomitantly measured. The ratio A_{343}/A_{329} is between 1.00 and 1.15.

B: To 20 mL of a dilution of Injection with water, containing about 20 mg of chloroquine hydrochloride, add 5 mL of trinitrophenol TS: a yellow precipitate is formed. Filter, wash the precipitate with water until the last washing is colorless, and dry over silica gel: the precipitate melts between 205 ° and 210°. [*Caution—Picrates may explode.*]

C: It responds to the tests for *Chloride* ⟨191⟩.

Bacterial endotoxins ⟨85⟩**—**It contains not more than 0.7 USP Endotoxin Unit per mg of chloroquine hydrochloride.

pH ⟨791⟩: between 5.5 and 6.5.

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

Assay—Transfer an accurately measured volume of Injection, equivalent to about 150 mg of chloroquine hydrochloride, to a 1000-mL volumetric flask, and dilute with water to volume. Transfer 5.0 mL of this solution to a 100-mL volumetric flask, add 10 mL of dilute hydrochloric acid (1 in 100), and dilute with water to volume. Dissolve an accurately weighed quantity of USP Chloroquine Phosphate RS in dilute hydrochloric acid (1 in 1000), and dilute quantitatively and stepwise with dilute hydrochloric acid (1 in 1000) to obtain a Standard solution having a known concentration of about 10 µg per mL. Concomitantly determine the absorbances of both solutions at the wavelength of maximum absorbance at about 343 nm, with a suitable spectrophotometer, using water as the blank. Calculate the quantity, in mg, of $C_{18}H_{26}ClN_3 \cdot 2HCl$ in the portion of Injection taken by the formula:

$$15.23C(A_U / A_S)$$

in which C is the concentration, in µg per mL, of USP Chloroquine Phosphate RS in the Standard solution; and A_U and A_S are the absorbances of the solution from the Injection and the Standard solution, respectively.

Chloroquine Phosphate

$C_{18}H_{26}ClN_3 \cdot 2H_3PO_4$ 515.86
1,4-Pentanediamine, N^4-(7-chloro-4-quinolinyl)-N^1,N^1-diethyl-, phosphate (1:2).
7-Chloro-4-[[4-(diethylamino)-1-methylbutyl]amino]quinoline phosphate (1:2) [50-63-5].

» Chloroquine Phosphate contains not less than 98.0 percent and not more than 102.0 per cent of $C_{18}H_{26}ClN_3 \cdot 2H_3PO_4$, calculated on the dried basis.

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩**—**
USP Chloroquine Phosphate RS
USP Hydroxychloroquine Sulfate RS

Identification—

A: It meets the requirements under *Identification—Organic Nitrogenous Bases* ⟨181⟩, chloroform being substituted for carbon disulfide in the test.

B: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 10 µg per mL.

Medium: dilute hydrochloric acid (1 in 1000).

Ratio: A_{343}/A_{329}, between 1.00 and 1.15.

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

Loss on drying ⟨731⟩**—**Dry it at 105 ° for 16 hours: it loses not more than 2.0% of its weight.

Assay—

Buffer solution—Accurately weigh about 13.6 g of monobasic potassium phosphate, and dissolve in 2 L of water. Add 2.0 mL perchloric acid, mix, and adjust with phosphoric acid to a pH of 2.5 ± 0.5. Pass the solution through a membrane filter having a 0.45-µm porosity.

Mobile phase—Prepare a mixture of *Buffer solution* and methanol (78:22). Make adjustments if necessar y (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Transfer an accurately weighed quantity of USP Chloroquine Phosphate RS to a suitable volumetric flask, and dissolve in and dilute with water to volume to obtain

a solution having a concentration of about 0.15 mg per mL of chloroquine phosphate.

Assay preparation—Transfer an accurately weighed quantity of Chloroquine Phosphate to a suitable volumetric flask, and dissolve in and dilute with water to volume to obtain a solution having a concentration of about 0.15 mg per mL of chloroquine phosphate.

System suitability solution—Transfer accurately weighed quantities of USP Hydroxychloroquine Sulfate RS and USP Chloroquine Phosphate RS to a suitable volumetric flask, and dissolve in and dilute with water to volume to obtain a solution having concentrations of about 0.015 mg per mL of hydroxychloroquine sulfate and 0.15 mg per mL of chloroquine phosphate.

Chromatography system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 224-nm detector and a 4.6-mm × 10-cm column that contains 5- µm packing L1. The flow rate is about 1.2 mL per minute. The column temperature is maintained at 25 ± 5°. Chromatograph the *System suitability solution,* and record the peak responses as directed for *Procedure:* the relative retention times are 1.0 for chloroquine phosphate and 0.8 for hydroxychloroquine sulfate; the resolution, *R,* between chloroquine phosphate and hydroxychloroquine sulfate is not less than 1.5; the column efficiency is not less than 2000 theoretical plates; for both compounds, the tailing factor is not more than 2.0; and the relative standard deviation is not more than 2.0%.

Procedure—Separately inject equal volumes (about 10 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 per centage of $C_{18}H_{26}ClN_3 \cdot 2H_3PO_4$ in the portion of Chloroquine Phosphate taken by the formula:

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

in which 100 is the per cent conversion factor; C_S is the concentration, in mg per mL, of USP Chloroquine Phosphate RS in the *Standard preparation;* C_U is the concentration, in mg per mL, of Chloroquine Phosphate in the *Assay preparation;* and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Chloroquine Phosphate Tablets

» Chloroquine Phosphate Tablets contain not less than 93.0 percent and not more than 107.0 percent of the labeled amount of $C_{18}H_{26}ClN_3 \cdot 2H_3PO_4$.

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩**—**
USP Amodiaquine Hydrochloride RS
USP Chloroquine Phosphate RS

Identification—A filtered solution of the Tablets meets the requirements of *Identification* tests *A* and *B* under *Chloroquine Hydrochloride Injection*.

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

Dissolution ⟨711⟩**—**

Medium: water; 900 mL.

Apparatus 2: 100 rpm.

Time: 45 minutes.

Procedure—Determine the amount of $C_{18}H_{26}ClN_3 \cdot 2H_3PO_4$ dissolved from UV 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 Chloroquine Phosphate RS in the same medium.

Tolerances—Not less than 75% *(Q)* of the labeled amount of $C_{18}H_{26}ClN_3 \cdot 2H_3PO_4$ is dissolved in 45 minutes.

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

Assay—

Buffer solution—Weigh about 13.6 g of monobasic potassium phosphate, and dissolve in 2 L of water. Add 2.0 mL of perchloric acid, mix, and adjust with phosphoric acid to a pH of 2.5. Pass the solution through a membrane filter having a 0.45-µm porosity.

Mobile phase—Prepare a mixture of *Buffer solution* and methanol (78:22). Make adjustments if necessar y (see *Chromatography* ⟨621⟩).

Standard preparation—Transfer an accurately weighed quantity of USP Chloroquine Phosphate RS to a suitable volumetric flask, and dissolve in and dilute with water to volume to obtain a solution having a known concentration of about 0.15 mg per mL of chloroquine phosphate.

Assay preparation—Weigh and finely powder 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 7.5 mg of chloroquine phosphate to a 50-mL volumetric flask, and dissolve in and dilute with water to volume. Sonicate for 20 minutes. Pass a portion of about 10 mL through a 0.2-µm nylon filter, discarding the first 4 mL, and use 2 mL for the analysis.

System suitability solution—Transfer an accurately weighed quantity of USP Amodiaquine Hydrochloride RS and USP Chloroquine Phosphate RS to a suitable volumetric flask, and dissolve in and dilute with water to volume to obtain a solution having known concentrations of about 0.15 mg per mL of amodiaquine hydrochloride and 0.15 mg per mL of chloroquine phosphate.

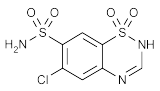
Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 224-nm detector and a 4.6-mm × 10-cm column that contains 5- µm packing L1. The flow rate is about 1.2 mL per minute. Chromatograph the *System suitability solution,* and record the peak responses as directed for *Procedure*: the relative retention times are 1.0 for chloroquine phosphate and 1.3 for amodiaquine hydrochloride; the resolution, *R,* between amodiaquine hydrochloride and chloroquine phosphate is not less than 1.5; the tailing factor for both compounds is not more than 1.5; and the relative standard deviation is not more than 2.0%.

Procedure—Separately inject equal volumes (about 10 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 percent of the label claim, of chloroquine phosphate ($C_{18}H_{26}ClN_3 \cdot 2H_3PO_4$) in the portion of Tablets taken by the formula:

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

in which 100 is the per cent conversion factor; C_S is the concentration, in mg per mL, of USP Chloroquine Phosphate RS in the *Standard preparation;* C_U is the concentration, in mg per mL, of chloroquine phosphate in the *Assay preparation,* based on the label claim; and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Chlorothiazide



$C_7H_6ClN_3O_4S_2$ 295.73