chloroquine contains not less than 98.0 percent and not more than 102.0 percent of C₁₈H₂₆ClN₃, 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: A₃₄₃ / A₃₂₉, 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 crystal violet TS, and titrate with 0.1 N perchloric acid, to a constant pink color. The absorbance is equivalent to 15.99 mg of C₁₈H₂₆ClN₃.

A solution of 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 absorbance 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 C₁₈H₂₆ClN₃ · 2HCl in the portion of Injection taken by the formula:

\[ 15.23(C/A_0) \]

in which C is the concentration, in µg per mL, of USP Chloroquine Phosphate RS in the Standard solution; and A₀ and A₁ are the absorbances of the solution from the Injection and the Standard solution, respectively.

Chloroquine Phosphate

C₁₈H₂₆ClN₃ · 2H₂PO₄ 513.86
1,4-Pentanediamine, N⁺-(7-chloro-4-quinolinyl)-N⁺,N⁺-diethylyl-dihydrochloride.

Chloroquine Phosphate contains not less than 98.0 percent and not more than 102.0 percent of C₁₈H₂₆ClN₃ · 2H₂PO₄, 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: A₃₄₃ / A₃₂₉, 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 perichloric 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-um porosity.

Mobile phase—Prepare a mixture of Buffer solution and methanol (78:22). Make adjustments if necessary (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°C. 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 cent of Chloroquine Phosphate taken by the formula:

\[
100\left(\frac{C_i}{C_0}\right)\left(\frac{r_0}{r_i}\right)
\]

in which 100 is the per cent conversion factor; \(C_i\) is the concentration, in mg per mL, of USP Chloroquine Phosphate RS in the Standard preparation; \(C_0\) is the concentration, in mg per mL, of Chloroquine Phosphate in the Assay preparation; and \(r_0\) and \(r_i\) 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 \(\text{C}_{18}\text{H}_{26}\text{ClN}_3\cdot\text{H}_2\text{PO}_4\). 

**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.

**A:** 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 \(\text{C}_{18}\text{H}_{26}\text{ClN}_3\cdot\text{H}_2\text{PO}_4\) 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 \(\text{C}_{18}\text{H}_{26}\text{ClN}_3\cdot\text{H}_2\text{PO}_4\) 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 necessary (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 powdered, 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 per cent of the label claim, of chloroquine phosphate (\(\text{C}_{18}\text{H}_{26}\text{ClN}_3\cdot\text{H}_2\text{PO}_4\)) in the portion of Tablets taken by the formula:

\[
100\left(\frac{C_i}{C_0}\right)\left(\frac{r_0}{r_i}\right)
\]

in which 100 is the per cent conversion factor; \(C_i\) is the concentration, in mg per mL, of USP Chloroquine Phosphate RS in the Standard preparation; \(C_0\) is the concentration, in mg per mL, of chloroquine phosphate in the Assay preparation, based on the label claim; and \(r_0\) and \(r_i\) are the peak responses obtained from the Assay preparation and the Standard preparation, respectively.

**Chlorothiazide**

\[
\text{C}_7\text{H}_6\text{ClN}_3\text{O}_4\text{S}_2 \quad 295.73
\]

C7H6ClN3O4S2 295.73