Primaquine Phosphate

\[ \text{C}_{15}\text{H}_{21}\text{N}_3\text{O} \cdot 2\text{H}_3\text{PO}_4 \quad 455.34 \]

1,4-Pentanediamine, \( N^4-(6\text{-methoxy-8-quinolinyl})-\), (±), phosphate (1:2);
(±)-8-[(4-Amino-1-methylbutyl)amino]-6-methoxyquinoline phosphate (1:2) \[63-45-6\].

**DEFINITION**

**Change to read:**

Primaquine Phosphate contains \*NLT 97.0\% and NMT 102.0\%\* (RB 1-Jan-2012) of primaquine phosphate \( (\text{C}_{15}\text{H}_{21}\text{N}_3\text{O} \cdot 2\text{H}_3\text{PO}_4) \), calculated on the dried basis.

**IDENTIFICATION**

- **A. INFRARED ABSORPTION** (197K); Meets the requirements
- **B.** The residue obtained by ignition meets the requirements of the test for pyrophosphate, as described in Identification Tests—General (191), Phosphate.
- **C.** The retention time of the major peak of the Sample solution corresponds to that of the Standard solution, as obtained in the Assay.

**ASSAY**

**Change to read:**

**PROCEDURE**

- **Mobile phase:** Acetonitrile, tetrahydrofuran, trifluoroacetic acid, and water (9: 1: 0.1: 90)
- **Standard solution:** 0.4 mg/mL of USP Primaquine Phosphate RS in Mobile phase. [NOTE—Sonicate with intermittent shaking to dissolve, if necessary.]
- **System suitability stock solution:** 0.4 mg/mL of USP Primaquine Related Compound A RS in Mobile phase
- **System suitability solution:** Transfer 1.0 mL of the System suitability stock solution to a 10-mL volumetric flask, and dilute with USP Primaquine Phosphate RS in Mobile phase to volume.
- **Sensitivity solution:** 0.2 µg/mL of USP Primaquine Phosphate RS from the Standard solution
- **Sample solution:** 0.4 mg/mL in Mobile phase. [NOTE—Sonicate with intermittent shaking to dissolve, if necessary.]

**Chromatographic system**

(See Chromatography (621), System Suitability.)

**Mode:** LC

**Detector:** UV 265 nm

**Column:** 4.6-mm × 75-mm; 3-µm packing L7

**Flow rate:** 1.5 mL/min

**Injection volume:** 10 µL

**Run time:** 3 times the retention time of primaquine

**System suitability**

- **Samples:** Standard solution, System suitability solution, and Sensitivity solution

**Suitability requirements**

- **Resolution:** NLT 2.5 between primaquine and primaquine related compound A, System suitability solution

**Relative standard deviation:** NMT 1.0\% for primaquine, Standard solution

**Signal-to-noise ratio:** NLT 10 for the primaquine peak, Sensitivity solution

**Analysis**

**Samples:** Standard solution and Sample solution

Calculate the percentage of primaquine phosphate \( (\text{C}_{15}\text{H}_{21}\text{N}_3\text{O} \cdot 2\text{H}_3\text{PO}_4) \) in the portion of Primaquine Phosphate taken:

\[
\text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_S}{C_U} \right) \times 100
\]

\( r_U = \text{peak response from the Sample solution} \)
\( r_S = \text{peak response from the Standard solution} \)
\( C_S = \text{concentration of USP Primaquine Phosphate RS in the Standard solution (mg/mL)} \)
\( C_U = \text{concentration of Primaquine Phosphate in the Sample solution (mg/mL)} \)

**Acceptance criteria:** \*97.0\%-102.0\* (RB 1-Jan-2012) on the dried basis\* USP35

**IMPURITIES**

**Change to read:**

**A. ORGANIC IMPURITIES**

Mobile phase, Standard solution, System suitability solution, Sensitivity solution, Sample solution, Chromatographic system, and System suitability: Proceed as directed in the Assay.

**Analysis**

**Sample:** Sample solution

Calculate the percentage of each impurity in the portion of Primaquine Phosphate taken:

\[
\text{Result} = \left( \frac{r_U}{r_S} \right) \times 100
\]

\( r_U = \text{peak response of each impurity from the Sample solution} \)
\( r_S = \text{peak response of primaquine phosphate from the Sample solution} \)

**Acceptance criteria:** See Table 1. Disregard any impurity peak less than 0.05\%.

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specified unidentified impurity</td>
<td>0.24</td>
<td>0.20</td>
</tr>
<tr>
<td>Specified unidentified impurity</td>
<td>0.29</td>
<td>0.60</td>
</tr>
<tr>
<td>Primaquine related compound A</td>
<td>0.80</td>
<td>2.0</td>
</tr>
<tr>
<td>Primaquine</td>
<td>1.0</td>
<td>—</td>
</tr>
<tr>
<td>Secamine (RB 1-Oct-2012)</td>
<td>1.8</td>
<td>0.80 (RB 1-Oct-2012)</td>
</tr>
<tr>
<td>Any other individual impurities</td>
<td>—</td>
<td>0.20</td>
</tr>
<tr>
<td>Total impurities</td>
<td>—</td>
<td>3.0</td>
</tr>
</tbody>
</table>

\*8-[(4-Aminopentyl)amino]-6-methoxyquinoline.

\*N^4-(6-Methoxyquinolin-8-yl)pentane-1,3-diamine.

\* USP35
SPECIFIC TESTS
• Loss on Drying (731)
  Analysis: Dry a sample at 105° for 2 h.
  Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS
• Packaging and Storage: Preserve in well-closed, light-resistant containers.

Change to read:
• USP Reference Standards (11)
  USP Primaquine Phosphate RS
  ▲ USP Primaquine Related Compound A RS
  8-[(4-Aminopenyl)amino]-6-methoxyquinoline.
  \( C_{13}H_{21}N_{3}O \) 259.35 ▲ USP35