Oseltamivir Phosphate Capsules

**DEFINITION**
Oseltamivir Phosphate Capsules contain Oseltamivir Phosphate equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of oseltamivir \((C_{16}H_{28}N_{2}O_{4} \cdot H_3PO_4)\).

**IDENTIFICATION**
- The retention times of the major peaks of the Sample solution correspond to those of the Standard solution, as obtained in the Assay.

**ASSAY**

**PROCEDURE**
Solution A: Dissolve 6.8 g of potassium dihydrogen phosphate in 980 mL of water. Adjust with 1 M potassium hydroxide solution to a pH of 6.0, and dilute with water to 1 L.

Mobile phase: Methanol, acetonitrile, and water (245:135:620)

Diluent: Methanol, acetonitrile, and 0.01 N phosphoric acid (245:135:620)

Standard solution: 1 mg/mL of USP Oseltamivir Phosphate RS in Diluent

Sample solution: Weigh the contents of 20 Capsules, and mix. Prepare the equivalent of about 1 mg of oseltamivir phosphate per mL, based on the label claim, by first dispersing a suitable portion of the powder in about 40% of the flask volume of Diluent, using an ultrasonic bath for about 20 min, and diluting with Diluent to volume. Centrifuge an aliquot of this solution, and use the supernatant.

**Chromatographic system**
(See Chromatography (621), System Suitability.)

Mode: LC
Detector: UV 207 nm
Column: 4.6-mm x 25-cm; packing L7
Column temperature: 50°C
Flow rate: 1.2 mL/min
Injection size: 15 μL

**System suitability**
Sample: Standard solution
Suitability requirements
- Tailing factor: NMT 2.0
- Relative standard deviation: NMT 2.0%

**Analysis**
Samples: Standard solution and Sample solution
Calculate the percentage of the labeled amount of oseltamivir \((C_{16}H_{28}N_{2}O_{4} \cdot H_3PO_4)\) in the portion of Capsules taken:

\[
\text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_S}{C_U} \right) \times \left( \frac{M_1}{M_2} \right) \times 100
\]

- \(r_U\) = peak response from the Sample solution
- \(r_S\) = peak response from the Standard solution
- \(C_S\) = concentration of USP Oseltamivir Phosphate RS in the Standard solution (mg/mL)
- \(C_U\) = concentration of oseltamivir in the Sample solution (mg/mL)
- \(M_1\) = molecular weight of oseltamivir, 312.40
- \(M_2\) = molecular weight of oseltamivir phosphate, 410.40

Acceptance criteria: 90.0%–110.0%

**PERFORMANCE TESTS**

**Change to read:**

- **DISSOLUTION** (711)
  Medium: 0.1 N hydrochloric acid; 900 mL
  Apparatus 2: 50 rpm
  Time: 20 min
  Detector: UV 240 nm

Standard solution: Prepare a solution in Medium having a known concentration of about 0.11 mg/mL of USP Oseltamivir Phosphate RS. Quantitatively dilute a portion of this solution with Medium to obtain a solution having a known concentration similar to the expected concentration in the solution under test.

Sample solution: Pass a portion of the solution under test through a suitable filter of 1-μm pore size.

Excipients solution: Suspend an amount of the placebo mixture equivalent to the weight of the excipients in one dosage unit and one empty Capsule shell in 900 mL of Medium. Heat to 37°C and filter.

**Analysis**
Samples: Medium, Standard solution, Sample solution, and Excipients solution
Determine the amount of oseltamivir phosphate \((C_{16}H_{28}N_{2}O_{4} \cdot H_2PO_4)\) dissolved by measuring the absorbance of the Sample solution and Excipients solution in comparison with the Standard solution, using the Medium as the blank. Calculate the percentage of oseltamivir phosphate dissolved:

\[
\text{Result} = \left[ \frac{(A_U - A_I) \times C_I \times V \times 100}{(A_S \times L)} \right]
\]

- \(A_U\) = absorbance of the Sample solution
- \(A_I\) = absorbance of the Excipients solution
- \(C_I\) = concentration of USP Oseltamivir Phosphate RS in the Standard solution
- \(V\) = volume of Medium, 900 mL
- \(A_S\) = absorbance of the Standard solution
- \(L\) = Capsule label claim for oseltamivir phosphate (mg)

**Tolerances:** NLT 95% (UB 1-Oct-2010) (Q) of the labeled amount of oseltamivir phosphate is dissolved.

**UNIFORMITY OF DOSAGE UNITS** (905): Meet the requirements.

**IMPURITIES**

**Change to read:**

**PROCEDURE**
Solution A, Mobile phase, Diluent, Standard solution, Sample solution, and Chromatographic system: Proceed as directed in the Assay.

**Analysis**
Samples: Standard solution and Sample solution
Calculate the percentage of individual impurities in the portion of Capsules taken:

\[
\text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_S}{C_U} \right) \times \left( \frac{1/F}{\left( \frac{M_1}{M_2} \right)} \right) \times 100
\]

- \(r_U\) = peak response of each individual impurity from the Sample solution
- \(r_S\) = peak response from the Standard solution
- \(C_S\) = concentration of USP Oseltamivir Phosphate RS in the Standard solution (mg/mL)
- \(C_U\) = nominal concentration of oseltamivir in the Sample solution (mg/mL)

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Oseltamivir

\[ F = \text{relative response factor from } \text{Table 1} \]
\[ M_1 = \text{molecular weight of oseltamivir, 312.40} \]
\[ M_2 = \text{molecular weight of oseltamivir phosphate, 410.40} \]

**Acceptance criteria:** See Table 1.

### Table 1 (Continued)

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Relative Response Factor</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impurity A(^a)</td>
<td>0.18</td>
<td>1.4</td>
<td>(\ast 2.0; \text{(RB 1-Oct-2010)})</td>
</tr>
<tr>
<td>Impurity B(^b)</td>
<td>0.49</td>
<td>2.7</td>
<td>0.3</td>
</tr>
<tr>
<td>Oseltamivir phosphate</td>
<td>1.00</td>
<td>1.0</td>
<td>—</td>
</tr>
<tr>
<td>Impurity C(^c)</td>
<td>1.45</td>
<td>0.9</td>
<td>(\ast 0.5; \text{(RB 1-Oct-2010)})</td>
</tr>
<tr>
<td>Individual unknown</td>
<td>—</td>
<td>1.0</td>
<td>0.2</td>
</tr>
</tbody>
</table>

\(^a\) (3\(R\),4\(R\),5\(S\))-4-Acetylamino-5-amino-3-(1-ethylpropoxy)-1-cyclohexene-1-carboxylic acid.

\(^b\) 4-Acetylamino-3-hydroxybenzoic acid ethyl ester.

\(^c\) (3\(R\),4\(R\),5\(S\))-4-Amino-5-acetylamino-3-(1-ethylpropoxy)-1-cyclohexene-1-carboxylic acid ethyl ester.

**ADDITIONAL REQUIREMENTS**

- **Packaging and Storage:** Preserve in well-closed containers. Store at 25\(^\circ\), excursions permitted between 15\(^\circ\) and 30\(^\circ\).
- **USP Reference Standards** (11)
  - USP Oseltamivir Phosphate RS\(^a\)/(SP3)