Amiodarone Tablets

DEFINITION
Amiodarone Tablets contain NLT 90% and NMT 110% of the labeled amount of amiodarone (C20H25N2O5Cl).

IDENTIFICATION
- A. UV Absorption (197U)
  Sample solution: Prepare as directed in the test for Dissolution.
  Standard solution: Prepare as directed in the test for Dissolution.
  Acceptance criteria: Meet the requirements
- B. The retention time of the major peak of the Sample solution corresponds to that of the Standard solution, as obtained in the Assay.

ASSAY
- PROCEDURE
  Buffer: Add 7.0 mL of triethylamine into a 1000-mL flask containing 900 mL of water. Adjust the solution with phosphoric acid to a pH of 3.0 ± 0.1. Dilute with water to the volume, and mix well.
  Mobile phase: Methanol, acetonitrile, and Buffer (35:15:50)
  System suitability solution: 0.02 mg/mL of USP Amlodipine Besylate RS and 0.002 mg/mL of USP Amlodipine Related Compound A RS in Mobile phase
  Standard solution: 0.02 mg/mL of amiodarone prepared from USP Amlodipine Besylate RS in Mobile phase
  Sample stock solution: Place 5 Tablets into a 500-mL volumetric flask. Add 50 mL of Mobile phase to the flask, and swirl to disintegrate the Tablets. Add 300 mL of Mobile phase, insert the stopper into the flask, and shake on a reciprocating shaker for 30 min. Dilute with Mobile phase to volume, and mix well.
  Sample solution: 0.02 mg/mL of amiodarone from Sample stock solution in Mobile phase. Pass the sample through a 0.45-μm pore size syringe tip filter.
  Chromatographic system
    - System suitability solution
      Sample: System suitability solution
      [NOTE—The run time is about three times the retention of [the amlodipine peak.]
      Resolution: NLT 8.5 between amiodarone and amiodarone related compound A
      Tailing factor: NMT 2.0 for both amiodarone and amiodarone related compound A
      Relative standard deviation: NLT 1.0% for amiodarone and NMT 5.0% for amiodarone related compound A
    Analysis
      Samples: Standard solution and Sample solution
      Calculate the percentage of the labeled amount of amiodarone (C20H25N2O5Cl) in the portion of Tablets taken:
      \[
      \text{Result} = \left( \frac{r_0}{r_1} \right) \times \left( \frac{C_0}{C_s} \right) \times 100
      \]
      where:
      - \(r_0\) = peak response of amiodarone from the Sample solution
      - \(r_1\) = peak response of amiodarone from the Standard solution
      - \(C_0\) = concentration of USP Amlodipine Besylate RS in the Standard solution (mg/mL)
      - \(C_s\) = nominal concentration of amiodarone in the Sample solution (mg/mL)
      Acceptance criteria: 90%–110%

PERFORMANCE TESTS
- Dissolution
  [NOTE—Do not expose any of the solutions to stainless steel because of the degradation of amiodarone.]
  Medium: 0.01 N hydrochloric acid; 500 mL
  Apparatus 2: 75 rpm. [NOTE—Use paddles covered with Teflon or made of any inert material except stainless steel.]
  Time: 30 min
  Standard stock solution A: 0.14 mg/mL of USP Amlodipine Besylate RS prepared by dissolving in methanol (4% of the volume of the flask). Dilute with Medium to volume.
  Standard stock solution B: Prepare as directed for Standard stock solution A.
  Standard solution A: Prepare in Medium to obtain solutions having concentrations based on Tablet strength as listed in Table 1.
  Standard solution B: Prepare in Medium to obtain solutions having concentrations based on Tablet strength as listed in Table 2.

<table>
<thead>
<tr>
<th>Tablet Strength</th>
<th>Standard Stock Used</th>
<th>Concentration of USP Amlodipine Besylate RS (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5 mg</td>
<td>Standard stock solution A</td>
<td>3.5</td>
</tr>
<tr>
<td>5 mg</td>
<td>Standard stock solution A</td>
<td>7</td>
</tr>
<tr>
<td>10 mg</td>
<td>Standard stock solution A</td>
<td>14</td>
</tr>
</tbody>
</table>

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</thead>
<tbody>
<tr>
<td>2.5 mg</td>
<td>Standard stock solution B</td>
<td>7</td>
</tr>
<tr>
<td>5 mg</td>
<td>Standard stock solution B</td>
<td>14</td>
</tr>
<tr>
<td>10 mg</td>
<td>Standard stock solution B</td>
<td>28</td>
</tr>
</tbody>
</table>

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-μm pore size.

Analysis: Determine the amount of amiodarone (C20H25N2O5Cl) dissolved by employing UV absorption at the wavelength of maximum absorbance at about 237 nm on portions of the Sample solution in comparison with the Standard solutions, using a 1-cm quartz cell. Calculate the absorbivity:

\[
A_{237}^{1%} cm = \frac{A_{237}}{\text{concentration}} \times (1000/100)
\]

at 237 nm for Standard solution A and Standard solution B:

\[
\text{Result} = \frac{A_s}{C_s} \times (1000/100)
\]

where:
- \(A_s\) = absorbance of the Standard solution
- \(C_s\) = concentration of USP Amlodipine Besylate RS in the Standard solution (mg/mL)

Calculate the percentage of the labeled amount of amiodarone (C20H25N2O5Cl) dissolved:

\[
\text{Result} = \frac{A_{\text{mean}} A_{237}^{1%}}{V/L} \times (1000/100) \times \left( \frac{M_s}{M_d} \right) \times 100
\]

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Amlodipine

\[ A_u \] = absorbance of the Sample solution
\[ \text{mean } A_{u} \] = average absorptivity of Standard solution A and Standard solution B
\[ V \] = volume of Medium, 500 mL
\[ L \] = label claim (mg/Tablet)
\[ M_{r1} \] = molecular weight of amlodipine, 408.9
\[ M_{r2} \] = molecular weight of amlodipine besylate, 567.05

Tolerances: NLT 75% of the labeled amount of amlodipine (C20H25N2O5Cl) is dissolved.

• Uniformity of Dosage Units (905): Meet the requirements

**IMPURITIES**

**Change to read:**

• Organic Impurities
  Buffer, Mobile phase, System suitability solution, Chromatographic system, and System suitability: Prepare as directed in the Assay.
  Standard solution: Use the System suitability solution.
  Sample solution: Place a suitable number of Tablets into a 25-mL volumetric flask to obtain a solution having a final nominal concentration of 0.4 mg/mL of amlodipine. Add about 10 mL of Mobile phase to the flask. Swirl to disintegrate the Tablet(s) followed by sonication for 5 min to completely dissolve, and then cool the sample to room temperature. Dilute with Mobile phase to volume. Stir for an additional 15 min using a magnetic stir bar, and pass the sample through a 0.45-µm pore size syringe tip filter, discarding the first 5 mL.
  Analysis
  Samples: Standard solution and Sample solution
  Calculate the percentage of amlodipine related compound A in the portion of Tablets taken:

\[
\text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_S}{C_U} \right) \times \left( \frac{M_{r1}}{M_{r2}} \right) \times 100
\]

\[ r_U \] = peak response of amlodipine related compound A from the Sample solution
\[ r_S \] = peak response of amlodipine from the Standard solution
\[ C_S \] = concentration of USP Amlodipine Related Compound A RS in the Standard solution (mg/mL)
\[ C_U \] = nominal concentration of amlodipine in the Standard solution (mg/mL)
\[ M_{r1} \] = molecular weight of amlodipine related compound A, 406.86
\[ M_{r2} \] = molecular weight of amlodipine besylate fumarate, 522.93

• Calculate the percentage of amlodipine glucose/galactose adduct or amlodipine lactose adduct, if present, in the portion of Tablets taken:

\[
\text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_S}{C_U} \right) \times \left( \frac{M_{r1}}{M_{r2}} \right) \times 100
\]

\[ r_U \] = peak response of the amlodipine glucose/galactose adduct or amlodipine lactose adduct in the Sample solution
\[ r_S \] = peak response of amlodipine in the Standard solution

**ADDITIONAL REQUIREMENTS**

• Packaging and Storage: Preserve in tight, light-resistant containers. Store at controlled room temperature.

**Change to read:**

• USP Reference Standards (11)
  USP Amlodipine Besylate RS
  USP Amlodipine Related Compound A RS
  3-Ethyl, 5-methyl [2-(2-aminoethoxymethyl)-4-(2-chlorophenyl)-6-methyl-3,5-pyridinedicarboxylate] fumarate.●(RB 1-Feb-2011)

\[ C_{20H25ClN2O5} \times \text{H}_{2} \text{O} \times \text{H}_{2} \text{O}_2 \] = 522.93 (RB 1-Feb-2011)