Niacin Extended-Release Tablets

**Type of Posting**  
Revision Bulletin

**Posting Date**  
31-Jul–2020

**Official Date**  
01–Aug–2020

**Expert Committee**  
Non-Botanical Dietary Supplements

**Reason for Revision**  
Compliance

In accordance with the Rules and Procedures of the 2015–2020 Council of Experts, the Non-Botanical Dietary Supplement Expert Committee has revised the Niacin Extended-Release Tablets monograph. The purpose for the revision is to add *Dissolution Test 6* to accommodate FDA-approved drug products with different tolerances than the existing dissolution tests. Due to the addition of a table in *Test 6*, a table in the test for *Organic Impurities* was renumbered and references to it were updated accordingly.

The Niacin Extended-Release Tablets Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Natalia Davydova, Senior Scientific Liaison (301-816-8328 or nd@usp.org)
Niacin Extended-Release Tablets

DEFINITION
Niacin Extended-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of niacin (C₆H₄NO). 

IDENTIFICATION
• A. 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
  Diluent: Methanol and water (82:18)
  Mobile phase: Methanol and water (82:18), adjusted with glacial acetic acid to a pH of 3.15 ± 0.05
  Standard solution: 250 µg/mL of USP Niacin RS, 50 µg/mL of USP 6-Hydroxynicotinic Acid RS, and 97.8 µg/mL of pyridine in Diluent
  Sample solution: Transfer a quantity of powder, equivalent to 50 mg of niacin from NLT 20 finely powdered Tablets, to a suitable flask, add Diluent, and stir for 2 h. Dilute with Diluent to a final concentration of 250 µg/mL of niacin.

Chromatographic system
(See Chromatography (621), System Suitability.)
Mode: LC
Detector: UV 260 nm
Column: 4.6-mm × 15-cm; 5-µm packing L8
Flow rate: 1.0 mL/min
Injection volume: 25 µL

System suitability
Sample: Standard solution

Suitability requirements
Resolution: NLT 1.5 between pyridine and 6-hydroxynicotinic acid, and NLT 1.5 between 6-hydroxynicotinic acid and niacin
Relative standard deviation: NMT 3.0% for each of the peaks

Analysis
Calculate the percentage of the labeled amount of niacin (C₆H₄NO₂) in the portion of Tablets taken:

\[ \text{Result} = \left( \frac{r_u}{r_s} \right) \times \left( \frac{C_s}{C_u} \right) \times 100 \]

\( r_u \) = peak area of niacin from the Sample solution
\( r_s \) = peak area of niacin from the Standard solution
\( C_s \) = concentration of USP Niacin RS in the Standard solution (mg/mL)
\( C_u \) = nominal concentration of niacin in the Sample solution (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS
Change to read:
• Dissolution (711)

Test 1
Medium: Water; 900 mL
Apparatus 1: 100 rpm
Times: 1, 3, 6, 9, 12, and 20 h; without Medium replacement. [Note—Withdraw the same volume at each time point.]

Solution A: Solution of sodium heptanesulfonate in acetic acid, methanol, and water (4:44:33:19), w/w
Mobile phase: Mixture of methanol, water, and Solution A (560:440:25)

Standard solution: USP Niacin RS at a known concentration in water in the range of 75–750 µg/mL
Sample solution: Filtered portion of the solution under test suitably diluted with Medium if necessary

Chromatographic system
(See Chromatography (621), System Suitability.)
Mode: LC
Detector: UV 254 nm
Column: 3.9-mm × 15-cm; 10-µm packing L1
Flow rate: 1.0 mL/min
Injection volume: 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

Determine, in mg/mL, the content of niacin \((\text{C}_6\text{H}_{14}\text{NO}_5)\) in the Medium at each time point:

\[
\text{Result} = \left(\frac{r_u}{r_s}\right) \times C_s \times D
\]

- \(r_u\) = peak area of niacin from the Sample solution
- \(r_s\) = peak area of niacin from the Standard solution
- \(C_s\) = concentration of USP Niacin RS in the Standard solution (mg/mL)
- \(D\) = dilution factor for the Sample solution

Calculate the percentage of the labeled amount of niacin \((\text{C}_6\text{H}_{14}\text{NO}_5)\) dissolved at each time point:

At 1 h:

\[
\text{Result}_1 = (C_1 \times V/L) \times 100
\]

At 3 h:

\[
\text{Result}_2 = [C_2 \times (V - V_s) + C_2 \times V_s] \times 100/L
\]

At 6 h:

\[
\text{Result}_3 = [C_3 \times (V - 2 \times V_s) + (C_2 + C_3) \times V_s] \times 100/L
\]

At 9 h:

\[
\text{Result}_4 = [C_4 \times (V - 3 \times V_s) + (C_2 + C_3 + C_4) \times V_s] \times 100/L
\]

At 12 h:

\[
\text{Result}_5 = [C_5 \times (V - 4 \times V_s) + (C_2 + C_3 + C_4 + C_5) \times V_s] \times 100/L
\]

At 20 h:

\[
\text{Result}_6 = [C_6 \times (V - 5 \times V_s) + (C_2 + C_3 + C_4 + C_5 + C_6) \times V_s] \times 100/L
\]

- \(C\) = as \(C_1, C_2, \ldots, C_6\), the content of niacin in the Medium at each time point (mg/mL)
- \(V\) = volume of Medium, 900 mL
- \(V_s\) = volume of sample withdrawn at each time point (mL)
- \(L\) = label claim (mg/Tablet)

**Tolerances:** The percentage of the labeled amount of niacin \((\text{C}_6\text{H}_{14}\text{NO}_5)\) dissolved at the times specified in Table 1, Table 2, and Table 3 conforms to Dissolution (711), Acceptance Table 2.

### Table 1. For Tablets Labeled to Contain 500 mg or Less/Tablet

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NMT 15</td>
</tr>
<tr>
<td>3</td>
<td>17–32</td>
</tr>
<tr>
<td>6</td>
<td>33–48</td>
</tr>
<tr>
<td>9</td>
<td>43–63</td>
</tr>
<tr>
<td>12</td>
<td>52–77</td>
</tr>
<tr>
<td>20</td>
<td>NLT 75</td>
</tr>
</tbody>
</table>

### Table 2. For Tablets Labeled to Contain 750 mg/Tablet

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NMT 15</td>
</tr>
<tr>
<td>3</td>
<td>16–31</td>
</tr>
<tr>
<td>6</td>
<td>31–46</td>
</tr>
<tr>
<td>9</td>
<td>42–62</td>
</tr>
<tr>
<td>12</td>
<td>51–76</td>
</tr>
<tr>
<td>20</td>
<td>NLT 75</td>
</tr>
</tbody>
</table>

### Table 3. For Tablets Labeled to Contain 1000 mg/Tablet

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NMT 15</td>
</tr>
<tr>
<td>3</td>
<td>15–30</td>
</tr>
<tr>
<td>Time (h)</td>
<td>Amount Dissolved (%)</td>
</tr>
<tr>
<td>---------</td>
<td>----------------------</td>
</tr>
<tr>
<td>6</td>
<td>30–45</td>
</tr>
<tr>
<td>9</td>
<td>40–60</td>
</tr>
<tr>
<td>12</td>
<td>50–75</td>
</tr>
<tr>
<td>20</td>
<td>NLT 75</td>
</tr>
</tbody>
</table>

**Test 2:** If the product complies with this test, the labeling indicates that it meets USP Dissolution Test 2.

**Acid stage medium:** 0.1 N hydrochloric acid; 900 mL

**Buffer stage medium:** 6.8 g of monobasic potassium phosphate and 0.89 g of sodium hydroxide pellets in 1000 mL of water. Adjust with diluted sodium hydroxide or phosphoric acid to a pH of 6.8; 900 mL.

**Apparatus 1:** 100 rpm

**Times:** 1, 4, 12, and 24 h: 1 and 4 h in the Acid stage medium; 12 and 24 h in the Buffer stage medium. Replace the volume withdrawn with the equal volume of medium preheated to 37 ± 0.5°C.

**Procedure:** After 4 h replace the Acid stage medium with the Buffer stage medium, and run the test for the times specified (additional 20 h for a total of 24 h).

[NOTE—Withdraw the same volume at each time point. Pass a portion of the solution through a suitable filter.]

**Standard stock solution:** 0.2 mg/mL of USP Niacin RS in water

**Standard solution 1:** Dilute Standard stock solution with Acid stage medium to a final concentration of 0.01 mg/mL of USP Niacin RS.

**Standard solution 2:** Dilute Standard stock solution with Buffer stage medium to a final concentration of 0.01 mg/mL of USP Niacin RS.

**Sample solution**
- For Tablets labeled to contain 500 mg: Dilute a filtered portion of the solution under test with appropriate dissolution medium 25-fold.
- For Tablets labeled to contain 750 mg: Dilute a filtered portion of the solution under test with appropriate dissolution medium 33-fold.
- For Tablets labeled to contain 1000 mg: Dilute a filtered portion of the solution under test with appropriate dissolution medium 50-fold.

**Instrumental conditions**
(See Ultraviolet-Visible Spectroscopy (857).)

**Mode:** UV

**Analytical wavelength:** 262 nm

**Path length:** 1 cm

**Blank:** Acid stage medium or Buffer stage medium

**Analysis**

**Samples:** Standard solution 1 or Standard solution 2 and Sample solution

Determine the concentration, in mg/mL, of niacin \( \text{(C}_6\text{H}_5\text{NO}_2) \) in the sample withdrawn from the vessel at each time point:

\[
Result = \frac{([\text{A}_U - \text{A}_B]/\text{A}_S) \times \text{C}_S \times D}{\text{A}_S}
\]

- \( \text{A}_U \) = absorbance of the Sample solution
- \( \text{A}_B \) = absorbance of the Blank
- \( \text{A}_S \) = absorbance of the Standard solution
- \( \text{C}_S \) = concentration of USP Niacin RS in the Standard solution (mg/mL)
- \( D \) = dilution factor for the Sample solution

Calculate the percentage of the labeled amount of niacin \( \text{(C}_6\text{H}_5\text{NO}_2) \) dissolved at each time point:

At 1 h:

\[
\text{Result}_1 = (\text{C}_1 \times V) \times 100/L
\]

At 4 h:

\[
\text{Result}_2 = (\text{C}_2 \times V + \text{C}_1 \times V_S) \times 100/L
\]

At 12 h:

\[
\text{Result}_3 = [(\text{C}_3 + \text{C}_2) \times V + \text{C}_1 \times V_S] \times 100/L
\]

At 24 h:

\[
\text{Result}_4 = [(\text{C}_4 + \text{C}_3) \times V + (\text{C}_2 + \text{C}_1) \times V_S] \times 100/L
\]

- \( C \) = as \( C_1 \) to \( C_4 \), the content of niacin in the related dissolution medium at each time point (mg/mL)
- \( V \) = volume of Medium, 900 mL
- \( V_S \) = volume of sample withdrawn at each time point (mL)
- \( L \) = label claim (mg/Tablet)

**Tolerances:** The percentage of the labeled amount of niacin \( \text{(C}_6\text{H}_5\text{NO}_2) \) dissolved at the times specified in Table 4 and Table 5 conforms to Dissolution (711), Acceptance Table 2.

**Table 4. For Tablets Labeled to Contain 500 mg/Tablet**
### Table 5. For Tablets Labeled to Contain 750 and 1000 mg/Tablet

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NMT 25</td>
</tr>
<tr>
<td>4</td>
<td>30–50</td>
</tr>
<tr>
<td>12</td>
<td>65–85</td>
</tr>
<tr>
<td>24</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

**Test 3:** If the product complies with this test, the labeling indicates that it meets USP **Dissolution Test 3**.

**Medium:** Water; 900 mL

**Apparatus 1:** 100 rpm

**Times:** 1, 3, 6, 9, 12, and 20 h; without Medium replacement

[Note—Withdraw the same volume at each time point. Pass a portion of the solution through a stainless steel filter.]

**Solution A:** 1 mg/mL of sodium 1-hexanesulfonate monohydrate in water

**Mobile phase:** Mixture of Solution A, *methanol*, and glacial acetic acid (840:150:10)

**Standard solution:** 

(L/900) mg/mL of USP Niacin RS in Medium, where L is the label claim in mg/Tablet

[Note—Use sonication for complete dissolution, if necessary.]

**Sample solution:** Filtered portion of the solution under test

**Chromatographic system**

(See *Chromatography*〈621〉, *System Suitability*.)

**Mode:** LC

**Sample cooler:** 10°

**Detector:** UV 262 nm

**Column:** 3.9-mm × 15-cm; 10-µm packing L1

**Column temperature:** 40°

**Flow rate:** 1.5 mL/min

**Injection volume:** 2 µL

**System suitability**

**Sample:** Standard solution

**Suitability requirements**

- Theoretical plates: NLT 1000
- Tailing factor: NMT 2.0
- Relative standard deviation: NMT 2.0%

**Analysis**

**Samples:** Standard solution and Sample solution

Determine the concentration, in mg/mL, of niacin (C<sub>6</sub>H<sub>5</sub>NO<sub>2</sub>) in the Medium at each time point:

Result<sub>U</sub> = peak area of niacin from the Sample solution

Result<sub>S</sub> = peak area of niacin from the Standard solution

C<sub>S</sub> = concentration of USP Niacin RS in the Standard solution (mg/mL)

Calculate the percentage of the labeled amount of niacin (C<sub>6</sub>H<sub>5</sub>NO<sub>2</sub>) dissolved at each time point:

At 1 h:

Result<sub>1</sub> = (C<sub>U</sub> × V/L) × 100

At 3 h:

Result<sub>2</sub> = [C<sub>2</sub> × (V − V<sub>3</sub>) + C<sub>1</sub> × V<sub>3</sub>] × 100/L

At 6 h:

Result<sub>3</sub> = [C<sub>2</sub> × (V − 2 × V<sub>3</sub>) + (C<sub>1</sub> + C<sub>2</sub>) × V<sub>3</sub>] × 100/L

At 9 h:

Result<sub>4</sub> = [C<sub>2</sub> × (V − 3 × V<sub>3</sub>) + (C<sub>1</sub> + C<sub>2</sub> + C<sub>3</sub>) × V<sub>3</sub>] × 100/L

At 12 h:

Result<sub>5</sub> = [C<sub>2</sub> × (V − 4 × V<sub>3</sub>) + (C<sub>1</sub> + C<sub>2</sub> + C<sub>3</sub> + C<sub>4</sub>) × V<sub>3</sub>] × 100/L
At 20 h:

\[ \text{Result}_6 = \left( C_6 \times (V - 5 \times V_S) + (C_1 + C_2 + C_3 + C_4 + C_5) \times V_S \right) \times \frac{100}{L} \]

- \( C \) = as \( C_1, C_2, \ldots, C_6 \), the content of niacin in the Medium at each time point (mg/mL)
- \( V \) = volume of Medium, 900 mL
- \( V_S \) = volume of sample withdrawn at each time point (mL)
- \( L \) = label claim (mg/Tablet)

**Tolerances:** The percentage of the labeled amount of niacin (C\(_6\)H\(_2\)NO\(_2\)) dissolved at the times specified in Table 6 and Table 7 conforms to Dissolution (711), Acceptance Table 2.

### Table 6. For Tablets Labeled to Contain 500 and 1000 mg/Tablet

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NMT 20</td>
</tr>
<tr>
<td>3</td>
<td>15–35</td>
</tr>
<tr>
<td>6</td>
<td>30–50</td>
</tr>
<tr>
<td>9</td>
<td>40–65</td>
</tr>
<tr>
<td>12</td>
<td>50–80</td>
</tr>
<tr>
<td>20</td>
<td>NLT 70</td>
</tr>
</tbody>
</table>

### Table 7. For Tablets Labeled to Contain 750 mg/Tablet

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NMT 16</td>
</tr>
<tr>
<td>3</td>
<td>15–35</td>
</tr>
<tr>
<td>6</td>
<td>30–50</td>
</tr>
<tr>
<td>9</td>
<td>40–65</td>
</tr>
<tr>
<td>12</td>
<td>50–75</td>
</tr>
<tr>
<td>20</td>
<td>NLT 75</td>
</tr>
</tbody>
</table>

**Test 4:** If the product complies with this test, the labeling indicates that it meets USP Dissolution Test 4.

**Medium:** Water; 900 mL

**Apparatus 1:** 100 rpm

**Times:** 1, 3, 6, 9, 12, and 24 h for Tablets labeled to contain 500 and 1000 mg/Tablet, and 1, 6, 12, and 24 h for Tablets labeled to contain 750 mg/Tablet; without Medium replacement

[Note—Withdraw the same volume at each time point. Pass a portion of the solution through a 0.45-µm PVDF membrane filter, discarding the first 2 mL of the filtrate.]

**Standard stock solution:** 0.5 mg/mL of USP Niacin RS in water

**Standard solution:** Dilute Standard stock solution with Medium to a final concentration of 0.02 mg/mL of USP Niacin RS.

**Sample solution**

- For Tablets labeled to contain 500 mg: Dilute a filtered portion of the solution under test with Medium 25-fold.
- For Tablets labeled to contain 750 mg: Dilute a filtered portion of the solution under test with Medium 40-fold.
- For Tablets labeled to contain 1000 mg: Dilute a filtered portion of the solution under test with Medium 50-fold.

**Instrumental conditions**

(See Ultraviolet-Visible Spectroscopy (857).)

**Mode:** UV

**Analytical wavelength:** 262 nm

**Path length:** 1 cm

**Blank:** Medium

**Analysis**

**Samples:** Standard solution and Sample solution

Determine the concentration, in mg/mL, of niacin (C\(_6\)H\(_2\)NO\(_2\)) in the sample withdrawn from the vessel at each time point:

\[ \text{Result} = \left( \frac{A_U - A_B}{A_S} \right) \times C_S \times D \]

- \( A_U \) = absorbance of the Sample solution
- \( A_B \) = absorbance of the Blank
- \( A_S \) = absorbance of the Standard solution
- \( C_S \) = concentration of USP Niacin RS in the Standard solution (mg/mL)
- \( D \) = dilution factor for the Sample solution
For Tablets labeled to contain 500 and 1000 mg: Calculate the percentage of the labeled amount of niacin (C₆H₄NO₂) dissolved at each time point:

At 1 h:
\[ \text{Result}_1 = \left( C_1 \times \frac{V}{L} \right) \times 100 \]

At 3 h:
\[ \text{Result}_2 = \left[ C_2 \times (V - V_3) + C_1 \times V_3 \right] \times 100/L \]

At 6 h:
\[ \text{Result}_3 = \left[ C_3 \times (V - 2 \times V_3) + (C_1 + C_2) \times V_3 \right] \times 100/L \]

At 9 h:
\[ \text{Result}_4 = \left[ C_4 \times (V - 3 \times V_3) + (C_1 + C_2 + C_3) \times V_3 \right] \times 100/L \]

At 12 h:
\[ \text{Result}_5 = \left[ C_5 \times (V - 4 \times V_3) + (C_1 + C_2 + C_3 + C_4) \times V_3 \right] \times 100/L \]

At 24 h:
\[ \text{Result}_6 = \left[ C_6 \times (V - 5 \times V_3) + (C_1 + C_2 + C_3 + C_4 + C_5) \times V_3 \right] \times 100/L \]

For Tablets labeled to contain 750 mg:
Calculate the percentage of the labeled amount of niacin (C₆H₄NO₂) dissolved at each time point:

At 1 h:
\[ \text{Result}_1 = \left( C_1 \times \frac{V}{L} \right) \times 100 \]

At 6 h:
\[ \text{Result}_2 = \left[ C_2 \times (V - V_3) + C_1 \times V_3 \right] \times 100/L \]

At 12 h:
\[ \text{Result}_3 = \left[ C_3 \times (V - 2 \times V_3) + (C_1 + C_2) \times V_3 \right] \times 100/L \]

At 24 h:
\[ \text{Result}_4 = \left[ C_4 \times (V - 3 \times V_3) + (C_1 + C_2 + C_3) \times V_3 \right] \times 100/L \]

\[ C = \text{as } C_1, C_2, \ldots, C_6, \text{ the content of niacin in the Medium at each time point (mg/mL)} \]
\[ V = \text{volume of Medium, 900 mL} \]
\[ V_S = \text{volume of sample withdrawn at each time point (mL)} \]
\[ L = \text{label claim (mg/Tablet)} \]

Tolerances: The percentage of the labeled amount of niacin (C₆H₄NO₂) dissolved at the times specified in Table 8, Table 9, and Table 10 conforms to Dissolution (711), Acceptance Table 2.

Table 8. For Tablets Labeled to Contain 500 mg/Tablet

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NMT 15</td>
</tr>
<tr>
<td>3</td>
<td>17–32</td>
</tr>
<tr>
<td>6</td>
<td>33–48</td>
</tr>
<tr>
<td>9</td>
<td>48–68</td>
</tr>
<tr>
<td>12</td>
<td>60–80</td>
</tr>
<tr>
<td>24</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

Table 9. For Tablets Labeled to Contain 750 mg/Tablet

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NMT 15</td>
</tr>
<tr>
<td>6</td>
<td>20–40</td>
</tr>
<tr>
<td>12</td>
<td>48–68</td>
</tr>
<tr>
<td>24</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

Table 10. For Tablets Labeled to Contain 1000 mg/Tablet

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NMT 15</td>
</tr>
</tbody>
</table>
**Test 5:** If the product complies with this test, the labeling indicates that it meets USP Dissolution Test 5.

**Medium:** Water; 900 mL

**Apparatus 1:** 100 rpm

**Times:** 1, 6, 12, and 24 h; without Medium replacement

[Note—Withdraw the same volume at each time point. Pass a portion of the solution through a 0.45-µm nylon membrane filter, discarding the first 2 mL of the filtrate.]

**Solution A:** 1.1 mg/mL of sodium 1-heptanesulfonate in water

**Mobile phase:** Mixture of Solution A and methanol (70:30)

**Standard solution:** 0.84 mg/mL of USP Niacin RS in water

[Note—Use sonication for complete dissolution, if necessary.]

**Sample solution:** Filtered portion of the solution under test

**Chromatographic system**

(See Chromatography (623), System Suitability.)

**Mode:** LC

**Detector:** UV 262 nm

**Column:** 4.6-mm × 25-cm; 5-µm packing L1

**Column temperature:** 30°

**Flow rate:** 1.0 mL/min

**Injection volume:** 5 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

Determine the concentration, in mg/mL, of niacin (C₁₈H₂₈NO₁₉) in the Medium at each time point:

Result = \( \frac{r_f}{r_s} \times C_S \)

\( r_f \) = peak area of niacin from the Sample solution

\( r_s \) = peak area of niacin from the Standard solution

\( C_S \) = concentration of USP Niacin RS in the Standard solution (mg/mL)

Calculate the percentage of the labeled amount of niacin (C₁₈H₂₈NO₁₉) dissolved at each time point:

At 1 h:

Result₁ = \( \left( C_f \times \frac{V}{L} \right) \times 100 \)

At 6 h:

Result₂ = \( \left( C_f \times \frac{V - 2V_s}{L} + C_f \times V_s \right) \times 100/L \)

At 12 h:

Result₃ = \( \left( C_f \times \frac{V - 2C_fV_s}{L} + C_f + C_s \times V_s \right) \times 100/L \)

At 24 h:

Result₄ = \( \left( C_f \times \frac{V - 3C_fV_s}{L} + C_f + C_s + C_d \times V_s \right) \times 100/L \)

\( C \) = as \( C_f \), ..., \( C_d \), the content of niacin in the Medium at each time point (mg/mL)

\( V \) = volume of Medium, 900 mL

\( L \) = label claim (mg/Tablet)

\( V_S \) = volume of sample withdrawn at each time point (mL)

**Tolerances:** The percentage of the labeled amount of niacin (C₁₈H₂₈NO₁₉) dissolved at the times specified in Table 11 and Table 12 conforms to Dissolution (711), Acceptance Table 2.

**Table 11. For Tablets Labeled to Contain 500 mg/Tablet**

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>12–27</td>
</tr>
<tr>
<td>6</td>
<td>25–45</td>
</tr>
<tr>
<td>9</td>
<td>35–55</td>
</tr>
<tr>
<td>12</td>
<td>50–70</td>
</tr>
<tr>
<td>24</td>
<td>NLT 80</td>
</tr>
<tr>
<td>Time (h)</td>
<td>Amount Dissolved (%)</td>
</tr>
<tr>
<td>---------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>1</td>
<td>NMT 20</td>
</tr>
<tr>
<td>6</td>
<td>30–50</td>
</tr>
<tr>
<td>12</td>
<td>50–75</td>
</tr>
<tr>
<td>24</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

Table 12. For Tablets Labeled to Contain 1000 mg/Tablet

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NMT 20</td>
</tr>
<tr>
<td>6</td>
<td>20–40</td>
</tr>
<tr>
<td>12</td>
<td>45–65</td>
</tr>
<tr>
<td>24</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

**Test 6:** If the product complies with this test, the labeling indicates that it meets USP Dissolution Test 6.

**Medium:** Water; 900 mL

**Apparatus 1:** 100 rpm

**Times:** 1, 6, 12, and 24 h. Replace the volume withdrawn with the equal volume of Medium preheated to 37 ± 0.5°C.

**Standard stock solution:** 0.44 mg/mL of USP Niacin RS in water

**Sample solution**

- For Tablets labeled to contain 500 mg: Dilute a filtered portion of the solution under test with dissolution medium 20-fold.
- For Tablets labeled to contain 750 mg: Dilute a filtered portion of the solution under test with dissolution medium 33-fold.
- For Tablets labeled to contain 1000 mg: Dilute a filtered portion of the solution under test with dissolution medium 40-fold.

**Instrumental conditions**

(See Ultraviolet-Visible Spectroscopy (857).)

**Mode:** UV

**Analytical wavelength:** 262 nm

**Path length:** 1 cm

**Blank:** Medium

**Analysis**

**Samples:** Standard solution and Sample solution

Determine the concentration, in mg/mL, of niacin (C₆H₅NO₂) in the sample withdrawn from the vessel at each time point:

\[
\text{Result} = \left(\frac{(A_U - A_B)}{A_S}\right) \times C_S \times D
\]

- \(A_U\) = absorbance of the Sample solution
- \(A_B\) = absorbance of the Blank
- \(A_S\) = absorbance of the Standard solution
- \(C_S\) = concentration of USP Niacin RS in the Standard solution (mg/mL)
- \(D\) = dilution factor for the Sample solution

Calculate the percentage of the labeled amount of niacin (C₆H₅NO₂) dissolved at each time point:

At 1 h:

\[
\text{Result}_1 = (C_1 \times V) \times 100/L
\]

At 6 h:

\[
\text{Result}_2 = (C_2 \times V + C_1 \times V) \times 100/L
\]

At 12 h:

\[
\text{Result}_3 = [C_2 \times V + (C_1 + C_2) \times V_S] \times 100/L
\]

At 24 h:

\[
\text{Result}_4 = [C_4 \times V + (C_1 + C_2 + C_3) \times V_S] \times 100/L
\]

- \(C\) = as \(C_1, ..., C_4\), concentration of niacin in the dissolution medium at each time point (mg/mL)
- \(V\) = volume of Medium, 900 mL
- \(V_S\) = volume of the sample withdrawn from the vessel and replaced at each time point (mL)
- \(L\) = label claim (mg/Tablet)
Tolerances: The percentage of the labeled amount of niacin (C6H5NO2) dissolved at the times specified in Table 13 conforms to Dissolution (711), Acceptance Table 2.

Table 13. For Tablets Labeled to Contain 500, 750, and 1000 mg/Tablet

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NMT 20</td>
</tr>
<tr>
<td>6</td>
<td>25–50</td>
</tr>
<tr>
<td>12</td>
<td>45–75</td>
</tr>
<tr>
<td>24</td>
<td>NLT 80 (RB 1-Aug-2020)</td>
</tr>
</tbody>
</table>

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

**IMPURITIES**

Change to read:

• **Organic Impurities**

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

Analysis

Samples: Standard solution and Sample solution

Calculate the percentage of 6-hydroxynicotinic acid or pyridine in the portion of Tablets taken:

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

- \( r_U \) = peak area of 6-hydroxynicotinic acid or pyridine from the Sample solution
- \( r_S \) = peak area of 6-hydroxynicotinic acid or pyridine from the Standard solution
- \( C_S \) = concentration of USP 6-Hydroxynicotinic Acid RS or pyridine in the Standard solution (µg/mL)
- \( C_U \) = nominal concentration of niacin in the Sample solution (µg/mL)

Calculate the percentage of any unspecified impurity in the portion of Tablets taken:

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

- \( r_U \) = peak area of each impurity from the Sample solution
- \( r_S \) = peak area of niacin from the Standard solution
- \( C_S \) = concentration of USP Niacin RS in the Standard solution (µg/mL)
- \( C_U \) = nominal concentration of niacin in the Sample solution (µg/mL)

Acceptance criteria: See Table 14 (RB 1-Aug-2020)

Table 14 (RB 1-Aug-2020)

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyridine</td>
<td>0.14</td>
<td>0.2</td>
</tr>
<tr>
<td>6-Hydroxynicotinic acid</td>
<td>0.64</td>
<td>0.2</td>
</tr>
<tr>
<td>Niacin</td>
<td>1.0</td>
<td>—</td>
</tr>
<tr>
<td>Any unspecified impurity</td>
<td>—</td>
<td>0.1</td>
</tr>
<tr>
<td>Total impurities</td>
<td>—</td>
<td>1.0</td>
</tr>
</tbody>
</table>

**ADDITIONAL REQUIREMENTS**

• **Packaging and Storage**: Preserve in tight containers.

• **Labeling**: When more than one Dissolution test is given, the labeling states the Dissolution test used only if Test 1 is not used.

• **USP Reference Standards** (11)
  - USP 6-Hydroxynicotinic Acid RS
  - USP Niacin RS

1 Commercially available from Waters Corporation as PIC B7 Reagent (Part #85103).

Page Information:

Not Applicable

DocID: