In accordance with the Rules and Procedures of the 2015-2020 Council of Experts, the Chemical Medicines Monographs 2 Expert Committee has revised the Olmesartan Medoxomil Tablets. The purpose for the revision is to add Dissolution Test 2 to accommodate the FDA approved drug products with different dissolution conditions and tolerance than the existing dissolution test. A Labeling section is also added. Because there is no 10-mg tablet product in the US market, Sample stock solution section in the Assay is revised to remove 10-mg tablet strength.

The Olmesartan Medoxomil Tablets Revision Bulletin supersedes the monograph that was scheduled to become official in the First Supplement to USP 40–NF 35. The Revision Bulletin will be incorporated in the First Supplement to USP 41–NF 36.

Should you have any questions, please contact Edith Chang, Scientific Liaison (301-816-8392 or vec@usp.org).
**Olmesartan Medoxomil Tablets**

**DEFINITION**
Olmesartan Medoxomil Tablets contain NLT 93.0% and NMT 105.0% of the labeled amount of olmesartan medoxomil (C₂₉H₃₀N₆O₆).

**IDENTIFICATION**
- **A.** The UV absorption spectra of the major peak of the Sample solution exhibit maxima and minima at the same wavelengths as those of the corresponding peak of the Standard solution, as obtained in the Assay.
- **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**

**Change to read:**

- **PROCEDURE**
  - Solution A: 3.1 g/L of formic acid
  - Solution B: Acetonitrile and Solution A (10:90)
  - Solution C: Acetonitrile and Solution A (90:10)
  - Mobile phase: See Table 1.

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Solution B (%)</th>
<th>Solution C (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>68.8</td>
<td>31.2</td>
</tr>
<tr>
<td>1.5</td>
<td>37.5</td>
<td>62.5</td>
</tr>
<tr>
<td>1.6</td>
<td>68.8</td>
<td>31.2</td>
</tr>
<tr>
<td>3.0</td>
<td>68.8</td>
<td>31.2</td>
</tr>
</tbody>
</table>

Diluent: Acetonitrile and water (60:40)
Standard solution: 40 μg/mL of USP Olmesartan Medoxomil RS in Diluent
Sample stock solution: Prepare solutions of nominal concentrations of olmesartan medoxomil in Diluent as follows. To NLT 10 Tablets for 5 mg and NLT 5 Tablets for 40-mg Tablet strength, add Diluent to volume. Sonicate with occasional shaking to disintegrate the Tablets completely, centrifuge the suspension, and use the supernatant.
Sample solution: Nominally 40 μg/mL of olmesartan medoxomil in Diluent from Sample stock solution
Chromatographic system
(See Chromatography (621), System Suitability.)
Mode: LC
Detector: UV 249 nm. For Identification B, use a diode array detector in the range of 200–400 nm.

**PERFORMANCE TESTS**

**Change to read:**

- **Dissolution (711)**
  - Test 1
    - Medium: pH 6.8 phosphate buffer (see Reagents, Indicators, and Solutions—Buffer Solutions)
    - For Tablets labeled to contain 5 mg: 500 mL
    - For Tablets labeled to contain 20 and 40 mg: 1000 mL
    - Apparatus 2: 50 rpm
    - Time: 30 min
    - Diluent: Acetonitrile and water (60:40)
    - Standard stock solution: 2 mg/mL of USP Olmesartan Medoxomil RS in Diluent
    - Standard solution: (L/V) mg/mL of USP Olmesartan Medoxomil RS in Medium, where \( L \) is the label claim in mg/Tablet and \( V \) is the volume of the Medium in mL from the Standard stock solution
    - Sample solution: Pass a portion of the solution under test through a glass fiber filter of 1.2-μm pore size.
    - Instrumental conditions
      (See Ultraviolet-Visible Spectroscopy (857).)
    - Mode: UV
    - Analytical wavelength: 258 nm
  - Cells
    - For Tablets labeled to contain 5 and 20 mg: 1 cm
    - For Tablets labeled to contain 40 mg: 0.5 cm
  - Blank: Medium
  - Analysis
    - Standard solution and Sample solution
      Calculate the percentage of the labeled amount of olmesartan medoxomil (C₂₉H₃₀N₆O₆) dissolved:
      \[
      \text{Result} = \left( \frac{A_U}{A_S} \right) \times C_S \times V \times (1/L) \times 100
      \]
      \( A_U \) = absorbance of the Sample solution
      \( A_S \) = absorbance of the Standard solution
      \( C_S \) = concentration of the Standard solution (mg/mL)
      \( V \) = volume of Medium (see Medium)
      \( L \) = label claim (mg/Tablet)
**Tolerances:** NLT 75% (Q) of the labeled amount of olmesartan medoxomil (C_{29}H_{30}N_{6}O_{6}) is dissolved.

**Sample solution:** Nominally 1 mg/mL of olmesartan medoxomil in Diluent prepared as follows. Dissolve a suitable number of Tablets in Diluent. Sonicate and/or shake occasionally to disintegrate the Tablets completely. Centrifuge and pass the supernatant through a suitable filter of 0.45-μm pore size.

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

**Mode:** LC

**Detector:** UV 250 nm

**Column:** 4.6-mm x 10-cm; 3.5-μm packing L7

**Column temperature:** 40 °C

**Flow rate:** 1 mL/min

**Injection volume:** 10 μL

**System suitability**

**Samples:** System suitability solution and Sensitivity solution

**Suitability requirements**

**Resolution:** NLT 5 between olmesartan medoxomil and olmesartan medoxomil related compound A, System suitability solution

**Relative standard deviation:** NMT 2.0% for both peaks, System suitability solution

**Signal-to-noise ratio:** NLT 30, Sensitivity solution

**Analysis**

**Samples:** Standard solution and Sample solution

Calculate the percentage of each degradation product in the portion of Tablets taken:

Result = \( \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_S}{C_U} \right) \times \left( \frac{1}{F} \right) \times 100 \)

\( r_U \) = peak response of each degradation product from the Sample solution

\( r_S \) = peak response of olmesartan medoxomil from the Standard solution

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

\( C_U \) = nominal concentration of olmesartan medoxomil in the Sample solution (mg/mL)

\( F \) = relative response factor (see Table 3)

**Acceptance criteria:** See Table 3. Disregard peaks below 0.1%.

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**Table 3**

<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>Olmesartan</td>
<td>0.2</td>
<td>1.0</td>
<td>2.5</td>
</tr>
<tr>
<td>Olmesartan medoxomil related</td>
<td>0.7</td>
<td>1.6</td>
<td>—</td>
</tr>
<tr>
<td>compound A(^{a})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Olmesartan dimer(^{b})</td>
<td>1.0</td>
<td>0.8</td>
<td>0.5</td>
</tr>
<tr>
<td>Olefinic impurity(^{c})</td>
<td>1.5</td>
<td>1.0</td>
<td>0.6</td>
</tr>
</tbody>
</table>

*1-[(2′-[(1H-Tetrazol-5-yl)biphenyl-4-yl)methyl]-4-(2-hydroxypropan-2-yl)-2-propyl-1H-imidazole-5-carboxylic acid.

\(^{a}\) This is a process-related impurity that is controlled in the drug substance.

\(^{b}\) 1-[(2′-[(1H-Tetrazol-5-yl)-1′-biphenyl]-4-yl)methyl]-4-(2-hydroxypropan-2-yl)-2-propyl-1H-imidazole-5-carboxylic acid.

\(^{c}\) 5-Methyl-2-oxo-1,3-dioxol-4-yl)methyl 1-[(2′-[(1H-tetrazol-5-yl)-1′-biphenyl]-4-yl)methyl]-4-(prop-1-ene-2-yl)-2-propyl-1H-imidazole-5-carboxylate.

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**Table 2**

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Solution A (%)</th>
<th>Solution B (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>75</td>
<td>25</td>
</tr>
<tr>
<td>10</td>
<td>75</td>
<td>25</td>
</tr>
<tr>
<td>35</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>45</td>
<td>0</td>
<td>100</td>
</tr>
</tbody>
</table>

**Diluent:** Acetonitrile and water (90:10)

**System suitability solution:** 0.01 mg/mL each of USP Olmesartan Medoxomil RS and USP Olmesartan Medoxomil Related Compound A RS in Diluent

**Standard solution:** 0.01 mg/mL of USP Olmesartan Medoxomil RS in Diluent

**Sensitivity solution:** 0.002 mg/mL of USP Olmesartan Medoxomil RS in Diluent from the Standard solution

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**Uniformity of dosage units (905):** Meet the requirements.
Table 3 (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>Any unspecified degradation product</td>
<td>—</td>
<td>1.0</td>
<td>0.2</td>
</tr>
<tr>
<td>Total degradation products</td>
<td>—</td>
<td>—</td>
<td>4.1</td>
</tr>
</tbody>
</table>

- 1-[(2′-(1H-Tetrazol-5-yl)biphenyl-4-yl)methyl]-4-(2-hydroxypropan-2-yl)-2-propyl-1H-imidazole-5-carboxylic acid.
- This is a process-related impurity that is controlled in the drug substance.
- 1-[(2′-(1H-Tetrazol-5-yl)biphenyl-4-yl)methyl]-4-(2-[1-(2′-((1H-tetrazol-5-yl)biphenyl-4-yl)methyl)-4-(2-hydroxypropan-2-yl)-2-propyl-1H-imidazole-5-carboxyloxy)propan-2-yl]-2-propyl-1H-imidazole-5-carboxylate.
- 1-(2′-(1H-Tetrazol-5-yl)biphenyl-4-yl)methyl-4-(prop-1-en-2-yl)-2-propyl-1H-imidazole-5-carboxylate.

**ADDITIONAL REQUIREMENTS**

- **PACKAGING AND STORAGE:** Preserve in well-closed containers. Store at controlled room temperature.

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**Add the following:**

- **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 Olmesartan Medoxomil RS
  - USP Olmesartan Medoxomil Related Compound A RS
  - 1-[(2′-(1H-Tetrazol-5-yl)biphenyl-4-yl)methyl]-4,4-dimethyl-2-propyl-1H-furo[3,4-d]imidazol-6(4H)-one.
  - C₂₄H₂₄N₆O₂ 428.49

**15 (USP40)**