Add the following:

<table>
<thead>
<tr>
<th>Lamotrigine Tablets</th>
</tr>
</thead>
</table>

**DEFINITION**
Lamotrigine Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of lamotrigine (C₉H₇Cl₂N₅).

**IDENTIFICATION**

- **A. ULTRAVIOLET ABSORPTION (197U)**
  
  *Standard solution:* 0.02 mg/mL of USP Lamotrigine RS in 0.01 N hydrochloric acid
  
  *Sample solution:* 0.02 mg/mL of lamotrigine from crushed powdered Tablets in 0.01 N hydrochloric acid
  
  **Acceptance criteria:** The spectra of the Standard solution and Sample solution exhibit maxima and minima at the same wavelengths.

- **B.** The retention time of the lamotrigine peak of the Sample solution corresponds to that of the Standard solution, as obtained in the Assay.

**ASSAY**

**Change to read:**

- **PROCEDURE**
  
  *Buffer:* 0.8 g/L of ammonium acetate. Adjust with glacial acetic acid to a pH of 4.5.
  
  *Mobile phase:* Methanol and Buffer (60:40)
  
  *Standard solution:* 0.05 mg/mL of USP Lamotrigine RS in Mobile phase
  
  *Sample solution:* Transfer an amount equivalent to 100 mg of lamotrigine from a portion of crushed Tablets (NLT 20% (88-1 May 2011)) to a suitable volumetric flask to obtain a nominal concentration of lamotrigine of 1.0 mg/mL. Dissolve in 70% of the flask volume of Mobile phase by sonication for 20 min. Dilute with Mobile phase to volume. Centrifuge the solution. Quantitatively dilute a suitable volume of centrifugate with Mobile phase to obtain a nominal concentration of 0.05 mg/mL of lamotrigine.
  
  **Chromatographic system**
  
  *(See Chromatography (621), System Suitability.)*
  
  **Mode:** LC
  
  **Detector:** UV 210 nm
  
  **Column:** 4.6-mm × 15-cm; 5-µm packing L1
  
  **Flow rate:** 1 mL/min
  
  **Injection size:** 10 µL
  
  **System suitability**
  
  **Sample:** Standard solution
  
  **Suitability requirements**
  
  **Tailing factor:** NMT 2.0 for lamotrigine
  
  **Relative standard deviation:** NMT 2.0% for lamotrigine
  
  **Analysis**
  
  **Samples:** Standard solution and Sample solution
  
  Calculate the percentage of the labeled amount of lamotrigine (C₉H₇Cl₂N₅) in the portion of Tablets taken:
  
  \[
  \text{Result} = \left( \frac{r_0}{r_s} \right) \times \left( \frac{C_s}{C_l} \right) \times 100
  \]
  
  \[r_0 = \text{peak response from the Sample solution}\]
  
  \[r_s = \text{peak response from the Standard solution}\]
  
  \[C_s = \text{concentration of USP Lamotrigine RS in the Standard solution (mg/mL)}\]
  
  \[C_l = \text{nominal concentration of lamotrigine in the Sample solution (mg/mL)}\]

**PERFORMANCE TESTS**

**Dissolution (711)**

- **Test 1**
  
  **Medium:** 0.1 N hydrochloric acid; 900 mL
  
  **Apparatus 2:** 50 rpm
  
  **Time:** 30 min
  
  Determine the amount of lamotrigine (C₉H₇Cl₂N₅) dissolved by using one of the following methods:

  **Spectrometric method**
  
  **Standard stock solution:** 0.15 mg/mL of USP Lamotrigine RS in Medium prepared as follows. Dissolve a suitable quantity in 5% of the flask volume of methanol, and then dilute with Medium to volume.
  
  **Standard solution:** L/1000 mg/mL of USP Lamotrigine RS from the Standard stock solution in Medium, where L is the label claim in mg/Tablet
  
  **Sample solution:** Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Dilute with Medium to obtain a final theoretical concentration of L/1000 mg/mL, where L is the label claim in mg/Tablet, assuming complete dissolution of the label claim.

  **Instrumental conditions**
  
  *(See Spectrophotometry and Light-Scattering (851),)*
  
  **Mode:** UV
  
  **Analytical wavelength:** 267 nm
  
  **Blank:** Medium
  
  **Analysis**
  
  Calculate the percentage of the labeled amount of lamotrigine (C₉H₇Cl₂N₅) dissolved:
  
  \[
  \text{Result} = \left( \frac{A_U}{A_V} \right) \times \left( \frac{C_s}{C_l} \right) \times V \times 100
  \]
  
  \[A_U = \text{absorbance of the Sample solution}\]
  
  \[A_V = \text{absorbance of the Standard solution}\]
  
  \[C_s = \text{concentration of the Standard solution (mg/mL)}\]
  
  \[C_l = \text{label claim (mg/Tablet)}\]
  
  \[V = \text{volume of Medium, 900 mL}\]

**Chromatographic method**

- **Buffer and Mobile phase:** Prepare as directed in the Assay.
  
  **Standard stock solution:** 0.5 mg/mL of USP Lamotrigine RS in Medium prepared as follows. Dissolve a suitable quantity in 15% of the flask volume of methanol, and then dilute with Medium to volume.
  
  **Standard solution:** L/1000 mg/mL of USP Lamotrigine RS from the Standard stock solution in Medium where L is the label claim in mg/Tablet
  
  **Sample solution:** Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

**Chromatographic system**

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

**Mode:** LC

**Column:** 4.6-mm × 15-cm; 5-µm packing L1

**Detector:** UV 310 nm

**Flow rate:** 1 mL/min

**Injection size:** See Table 1.

<table>
<thead>
<tr>
<th>Label Claim (mg/Tablet)</th>
<th>Injection Size (µL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>50</td>
</tr>
<tr>
<td>100, 150, 200</td>
<td>10</td>
</tr>
</tbody>
</table>

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2 Lamotrigine

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

Analysis
Samples: Standard solution and Sample solution
Calculate the percentage of the labeled amount of lamotrigine (C₉H₇Cl₂N₅) dissolved:

\[ \text{Result} = \left( \frac{r_o}{r_s} \right) \times \left( \frac{C_s}{L} \right) \times V \times 100 \]

where:
- \( r_o \) = peak response from the Sample solution
- \( r_s \) = peak response from the Standard solution
- \( C_s \) = concentration of the Standard solution (mg/mL)
- \( L \) = label claim (mg/Tablet)
- \( V \) = volume of Medium, 900 mL

Tolerances: NLT 80% (Q) of the labeled amount of lamotrigine is dissolved.

Test 2: If the product complies with this test, the labeling indicates that it meets USP Dissolution Test 2.
Medium, Apparatus, and Time: Proceed as directed for Test 1.
Analysis: Determine the amount of lamotrigine dissolved using either the Spectrophotometric method or Chromatographic method described in Test 1.
Tolerances: NLT 75% (Q) of the labeled amount of lamotrigine is dissolved.

Test 3: If the product complies with this test, the labeling indicates that it meets USP Dissolution Test 3.
Medium: 0.1 N hydrochloric acid; 900 mL
Apparatus 2: 50 rpm
Time: 15 min
Standard solution: (L/900) mg/mL of USP Lamotrigine RS in Medium, where L is the tablet label claim in mg
Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-μm pore size.

Instrumental conditions
(See Spectrophotometry and Light-Scattering (851).)
Mode: UV
Analytical wavelength: 270 nm
Cell
For Tablets labeled to contain 100, 150, or 200 mg: 0.2-cm flow cell
For Tablets labeled to contain 25 mg: 1 cm
Blank: Medium

Analysis
Samples: Standard solution and Sample solution
Calculate the percentage of the labeled amount of lamotrigine (C₉H₇Cl₂N₅) dissolved:

\[ \text{Result} = \left( \frac{A_o}{A_s} \right) \times \left( \frac{C_s}{L} \right) \times V \times 100 \]

where:
- \( A_o \) = absorbance of the Sample solution
- \( A_s \) = absorbance of the Standard solution
- \( C_s \) = concentration of the Standard solution (mg/mL)
- \( L \) = label claim (mg/Tablet)
- \( V \) = volume of Medium, 900 mL

Tolerances: NLT 80% (Q) of the labeled amount of lamotrigine is dissolved.

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

Impurities

Change to read:

• Organics Impurities
Buffer: Prepare as directed in the Assay.
Mobile phase: Acetonitrile, methanol, and Buffer (10:30:60)
Diluent: Methanol and Buffer (60:40)
System suitability solution: 1 μg/mL of Lamotrigine Related Compound B RS and 0.4 mg/mL of USP Lamotrigine RS in Diluent
Standard solution: 1.0 μg/mL of USP Lamotrigine RS in Diluent
Sample solution: Transfer an amount equivalent to 100 mg of lamotrigine from a portion of crushed Tablets (NLT 20) to a suitable volumetric flask to obtain a nominal concentration of lamotrigine of about 0.4 mg/mL. Dissolve in 70% of the flask volume of Mobile phase by sonication and shaking intermittently for 30 min. Dilute with Diluent to volume. Pass through a membrane filter of 0.45-μm pore size.

Chromatographic system
(See Chromatography (621), System Suitability.)
Mode: LC
Detector: UV 210 nm
Column: 4.6-mm × 25-cm; 5-μm packing L1
Flow rate: 1 mL/min
Injection size: 5 µL

System suitability
Samples: System suitability solution and Standard solution
Suitability requirements
Resolution: NLT 2.0 between lamotrigine related compound B and lamotrigine, System suitability solution
Tailing factor: NMT 2.0 for lamotrigine, Standard solution
Relative standard deviation: NMT 10.0% for lamotrigine, Standard solution

Analysis
Samples: Standard solution and Sample solution
Calculate the percentage of any individual impurity in the portion of Tablets taken:

\[ \text{Result} = \left( \frac{r_o}{r_s} \right) \times \left( \frac{C_s}{C_o} \right) \times \left( \frac{1}{F} \right) \times 100 \]

where:
- \( r_o \) = peak response of each individual impurity from the Sample solution
- \( r_s \) = peak response of lamotrigine from the Standard solution
- \( C_s \) = concentration of USP Lamotrigine RS in the Standard solution (mg/mL)
- \( C_o \) = nominal concentration of lamotrigine in the Sample solution (mg/mL)
- \( F \) = relative response factor for the corresponding impurity (see Table 2)

Acceptance criteria: See Table 2.
Table 2

<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>Lamotrigine related compound B&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.67</td>
<td>0.75</td>
<td>0.2</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>1.0</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Lamotrigine related compound C&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.5</td>
<td>1.0</td>
<td>0.5</td>
</tr>
<tr>
<td>Any individual unspecified degradation impurity</td>
<td>—</td>
<td>1.0</td>
<td>0.2</td>
</tr>
<tr>
<td>Total impurities</td>
<td>—</td>
<td>—</td>
<td>0.75</td>
</tr>
</tbody>
</table>

<sup>a</sup> 2,3-Dichlorobenzoic acid.
<sup>b</sup> 3-Amino-6-(2,3-dichlorophenyl)-1,2,4-triazin-5(4H)-one.

**ADDITIONAL REQUIREMENTS**

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

- **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 Lamotrigine RS
  - USP Lamotrigine Related Compound B RS
  - 2,3-Dichlorobenzoic acid.
  - C<sub>7</sub>H<sub>4</sub>Cl<sub>2</sub>O<sub>2</sub> 191.01<sup>USP34</sup>