Mycophenolate Mofetil Capsules

**DEFINITION**
Mycophenolate Mofetil Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of mycophenolate mofetil (C23H31NO7).

**IDENTIFICATION**
- **A. ULTRAVIOLET ABSORPTION (197U)**
  - **Standard solution** and **Sample solution**: Use the **Standard solution** and **Sample solution** as prepared in the **Assay** test.
  - **Acceptance criteria**: The UV absorption spectra of the **Standard solution** and **Sample solution** exhibit maxima and minima at the same wavelength within ±3 nm.
- **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**
  - **Phosphoric acid solution**: Phosphoric acid and water (3:50).
  - **Triethylamine solution**: Transfer 3 mL of triethylamine to 1000 mL of water. Adjust with **Phosphoric acid solution** to a pH of 5.3.
  - **Mobile phase**: Acetonitrile and Triethylamine solution (11:9).
  - **Standard solution**: 0.125 mg/mL of USP Mycophenolate Mofetil RS in acetonitrile.
  - **Sample solution**: Open Capsules, equivalent to 1.25 g of mycophenolate mofetil based on the label claim, and transfer the contents including Capsule shells into a 500-mL volumetric flask. Add 50 mL of water, and shake mechanically for a minimum of 15 min. Add 350 mL of acetonitrile, sonicate for 15 min, and shake mechanically for 20 min. Dilute with acetonitrile to volume. Transfer 5.0 mL of this solution to a 100-mL volumetric flask. Add 50 mL of water, and labeling indicates that the product meets USP Dissolution Test 1.
  - **System suitability**
    - **Sample solution**: 40 rpm, with sinker. Time: 20 min.
    - **Standard solution**: 0.278 mg/mL of USP Mycophenolate Mofetil RS in Medium.
    - **Sample solution**: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.
  - **Detector**: UV 250 nm.
  - **Path length**: 0.1 cm.
  - **Blank**: Medium.
  - **Analysis**
    - **Samples**: **Standard solution** and **Sample solution**.
    - **Calculation**: Calculate the percentage of the labeled amount of mycophenolate mofetil (C23H31NO7) dissolved:
      
      \[
      \text{Result} = \left( \frac{A_U}{A_S} \right) \times (C_S/L) \times V \times 100
      \]

      \[A_U = \text{absorbance of the Sample solution}\]

      \[A_S = \text{absorbance of the Standard solution}\]

      \[C_S = \text{concentration of the Standard solution (mg/mL)}\]

      \[L = \text{label claim (mg/Capsule)}\]

      \[V = \text{volume of Medium, 900 mL}\]

    - **Tolerances**: NLT 80% (Q) of the labeled amount of mycophenolate mofetil (C23H31NO7) is dissolved.

- **Test 2**: If the product complies with this test, the labeling indicates that the product meets USP Dissolution Test 2.
  - **Medium**: 0.1 N hydrochloric acid; 900 mL.
  - **Apparatus 2**: 40 rpm, with sinker.
  - **Time**: 30 min.
  - **Standard solution**: 0.028 mg/mL of USP Mycophenolate Mofetil RS in Medium.
  - **Sample solution**: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Discard the first 3–5 mL, and dilute 1 mL of the filtrate with Medium to 10 mL.

**Instrumental conditions**
(See Spectrophotometry and Light-Scattering (851)).
- **Mode**: UV.
- **Analytical wavelength**: 250 nm.
- **Blank**: Medium.
- **Analysis**
    - **Samples**: **Standard solution** and **Sample solution**.
    - **Calculation**: Calculate the percentage of the labeled amount of mycophenolate mofetil (C23H31NO7) dissolved:
      
      \[
      \text{Result} = \left( \frac{A_U}{A_S} \right) \times (C_S/L) \times V \times (D/(1/L)) \times 100
      \]

      \[A_U = \text{absorbance of the Sample solution}\]

      \[A_S = \text{absorbance of the Standard solution}\]

      \[C_S = \text{concentration of the Standard solution (mg/mL)}\]

      \[L = \text{label claim (mg/Capsule)}\]

      \[V = \text{volume of Medium, 900 mL}\]

      \[D = \text{dilution factor, 10}\]

      \[L = \text{label claim (mg/Capsule)}\]

    - **Tolerances**: NLT 80% (Q) of the labeled amount of mycophenolate mofetil (C23H31NO7) is dissolved.

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

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IMPURITIES

Change to read:

- **LIMIT OF DEGRADATION PRODUCTS**
  - Mobile phase, Standard solution, Sample solution, and Chromatographic system: Proceed as directed in the Assay.
  - Sensitivity solution: 0.0625 µg/mL of USP Mycophenolate Mofetil RS in acetonitrile
  - System suitability
    - Samples: Standard solution and Sensitivity solution
    - Suitability requirements
      - Signal-to-noise ratio: NLT 10, Sensitivity solution
      - Tailing factor: NMT 2.0, Standard solution
      - Relative standard deviation: NMT 2.0%, Standard solution

  **Analysis**
  - [NOTE—The run time for the Sample solution is three times that of the retention time of the mycophenolate mofetil peak.]
  - Samples: Standard solution and Sample solution
  - Calculate the percentage of each impurity in the portion of Capsules taken:
    \[
    \text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_S}{C_U} \times \left( 1/1 \right) \right) \times 100
    \]
  - Where:
    - \( r_U \) = peak response of each individual impurity from the Sample solution
    - \( r_S \) = peak response of mycophenolate mofetil from the Standard solution
    - \( C_S \) = concentration of USP Mycophenolate Mofetil RS in the Standard solution (mg/mL)
    - \( C_U \) = nominal concentration of mycophenolate mofetil in the Sample solution (mg/mL)
    - \( F \) = relative response factor for each individual impurity (see Table 1)

  **Acceptance criteria:** See Table 1. Disregard peaks at relative retention times of 1.45 and 2.15. Disregard any peaks less than 0.05%.

<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>Mycophenolic acid</td>
<td>0.6</td>
<td>1.4</td>
<td><em>1.0</em> (RB 1-May 2011)</td>
</tr>
<tr>
<td>Mycophenolate N-oxide analog*</td>
<td>0.8</td>
<td>1.0</td>
<td>0.2</td>
</tr>
<tr>
<td>Mycophenolate mofetil</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any single unspecified impurity</td>
<td>1.0</td>
<td>1.0</td>
<td>0.1</td>
</tr>
<tr>
<td>Total degradation products</td>
<td></td>
<td></td>
<td><em>1.5</em> (RB 1-May 2011)</td>
</tr>
</tbody>
</table>

* (Z)-6-(1,3-Dihydro-4-hydroxy-6-methoxy-7-methyl-3-oxo-5-isobenzofuranyl)-4-methyl-4-hexenoic acid.
* 2-Morpholinooethyl (Z)-6-(1,3-dihydro-4-hydroxy-6-methoxy-7-methyl-3-oxo-5-isobenzofuranyl)-4-methyl-4-hexenoate N-oxide.

- **LIMIT OF Z-MYCOPHENOLATE MOFETIL**
  - [NOTE—Z-Mycophenolate mofetil is 2-morpholinooethyl (Z)-6-(4-hydroxy-6-methoxy-7-methyl-3-oxo-5-phthalanyl)-4-methyl-4-hexenoate N-oxide.]
  - Triethylamine solution: Proceed as directed in the Assay.
  - Mobile phase: Acetonitrile and Triethylamine solution (7:13)

**Standard solution:** 0.025 mg/mL of USP Mycophenolate Mofetil RS in acetonitrile

**Sensitivity solution:** 1.25 µg/mL of USP Mycophenolate Mofetil RS in acetonitrile

**Sample solution:** Open Capsules, equivalent to 1.25 g of mycophenolate mofetil based on the label claim, and transfer the contents including Capsule shells into a 500-mL volumetric flask. Add 50 mL of water, and shake mechanically for a minimum of 15 min. Add 350 mL of acetonitrile, sonicate for 15 min, and shake mechanically for 20 min. Dilute with acetonitrile to volume. Pass through a nylon filter of 0.45-µm pore size, and discard the first 2 mL of the filtrate.

**Chromatographic system**
  - (See Chromatography (621), System Suitability.)
  - **Mode:** LC
  - **Detector:** UV 215 nm
  - **Column:** 4.6-mm × 15-cm; 3.5-µm packing L7
  - **Column temperature:** 60°C
  - **Flow rate:** 1.5 mL/min
  - **Injection volume:** 10 µL
  - **Run time:** 1.7 times the retention time of the mycophenolate mofetil peak

**System suitability**
  - Samples: Standard solution and Sensitivity solution
  - Calculate the percentage of Z-mycophenolate mofetil in the portion of Capsules taken:
    \[
    \text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_S}{C_U} \times \left( 1/1 \right) \right) \times 100
    \]
  - Where:
    - \( r_U \) = peak response of Z-mycophenolate mofetil from the Sample solution
    - \( r_S \) = peak response of mycophenolate mofetil from the Standard solution
    - \( C_S \) = concentration of USP Mycophenolate Mofetil RS in the Standard solution (mg/mL)
    - \( C_U \) = nominal concentration of mycophenolate mofetil in the Sample solution (mg/mL)

  **Acceptance criteria**
  - Z-Mycophenolate mofetil: NMT 0.10%

**ADDITIONAL REQUIREMENTS**

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

**Add the following:**

- **LABELING:** When more than one Dissolution test is given, the labeling states the test used only if Test 1 is not used.
- **USP REFERENCE STANDARDS** (11)
  - USP Mycophenolate Mofetil RS

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