**Mycophenolate Mofetil Tablets**

**DEFINITION**
Mycophenolate Mofetil Tablets 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 test for Dissolution.
  
  Acceptance criteria: The UV absorption spectrum of the Standard solution and the Sample solution exhibit maxima and minima at the same wavelength within ±3 nm.

- **B.** The retention time of the major peak in 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:** Add 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:** Place Tablets, equivalent to 2.5 g of mycophenolate mofetil based on the label claim, into a 1000-mL volumetric flask. Add 100 mL of water and shake mechanically for a minimum of 15 min. Add 700 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, and dilute with acetonitrile to volume. Pass through a 0.45-µm pore size filter, and discard the first 5 mL of filtrate.

**Chromatographic system**

(See Chromatography (621), System Suitability.)

- **Mode:** LC
- **Detector:** UV 250 nm
- **Column:** 4.6-mm × 25-cm; 5-µm packing L7
- **Column temperature:** 45°
- **Auto sampler temperature:** 10° ± 5°
- **Flow rate:** 1.5 mL/min
- **Injection size:** 20 µL

**System suitability**

- **Sample:** Standard solution
- **Suitability requirements**
- **Tailing factor:** NMT 2
- **Relative standard deviation:** NMT 2.0%

**Analysis**

- **Samples:** Standard solution and Sample solution
- **Calculate the percentage of mycophenolate mofetil (C23H31NO7) in the portion of Tablets taken:**
  
  Result = \( \left( \frac{r_s}{r_i} \right) \times \left( \frac{C_s}{C_l} \right) \times 100 \)

  \( r_s \) = peak response from the Sample solution

  \( r_i \) = peak response from the Standard solution

  \( C_s \) = concentration of USP Mycophenolate Mofetil RS in the Sample solution (mg/mL)

  \( C_l \) = nominal concentration of mycophenolate mofetil in the Sample solution (mg/mL)

  **Acceptance criteria:** 90.0%–110.0%

**PERFORMANCE TESTS**

**Change to read:**

- **Dissolution (711)**
  
  *Test 1* (8B 14-Feb-2011)

  - **Medium:** 0.1 N hydrochloric acid; 900 mL
  - **Apparatus 2:** 50 rpm
  - **Times:** 5 and 15 min
  - **Standard solution:** 0.55 mg/mL of USP Mycophenolate Mofetil RS in Medium
  - **Sample solution:** Pass a portion of the solution under test through a suitable 0.45-µm pore size filter.
  - **Detector:** UV 304 nm
  - **Path length:** 0.1 cm
  - **Blank:** Medium

  **Analysis:** Calculate the percentage of mycophenolate mofetil (C23H31NO7) dissolved:

  \[
  \left( \frac{A_S}{A_L} \right) \times \left( \frac{C_L}{L} \right) \times \frac{V}{V_{100}} = \frac{\text{correction factor}}{\text{per centage dissolved at 5 min}}
  \]

  \( A_S \) = absorbance of the Sample solution

  \( A_L \) = absorbance of the Standard solution

  \( C_L \) = concentration of the Standard solution (mg/mL)

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

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

  **Correction factor:** \( \left( \frac{V \times P_S}{V} \right) \times 100 \)

  \( P_S \) = percentage of mycophenolate dissolved at 5 min

  **Result:** Correction factor + percentage dissolved at 15 min

**Tolerances:** NLT 75% (Q) of the labeled amount of mycophenolate mofetil (C23H31NO7) is dissolved in 5 min, and NLT 85% of the labeled amount of mycophenolate mofetil (C23H31NO7) is dissolved in 15 min.

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

- **Medium:** 0.1 N hydrochloric acid; 900 mL, deaerated
- **Apparatus 2:** 50 rpm
- **Times:** 5 and 15 min
- **Diluted phosphoric acid:** Transfer 5 mL of phosphoric acid to a 25-mL volumetric flask. Dilute with water to volume.
- **Buffer:** 3.0 mL/L of triethylamine in water. Adjust with Diluted phosphoric acid to a pH of 5.3.

**Mobile phase:** Acetonitrile and Buffer (45:55)

**Diluent:** Acetonitrile and Buffer (20:80)

**Standard stock solution:** 0.56 mg/mL of USP Mycophenolate Mofetil RS in Medium

**Standard solution:** Dilute the Standard stock solution with Diluent to obtain a final concentration of 0.11 mg/mL.

**Sample solution:** Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Transfer 5 mL of the filtrate to a 25-mL volumetric flask, and dilute with Diluent to volume.

**Chromatographic system**

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

**Mode:** LC  
**Detector:** UV 250 nm  
**Column:** 4.6-mm × 15-cm; 5-µm packing L7  
**Column temperature:** 35°  
**Flow rate:** 1.5 mL/min  
**Injection size:** 20 µL  

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

**Analysis:** Calculate the percentage of mycophenolate mofetil \((C_{23}H_{31}NO_{7})\) dissolved:

\[
\text{Result} = \left( \frac{r_0}{r_L} \right) \times \left( \frac{C_S}{C_L} \right) \times V \times 100
\]

where:
- \(r_0\) = peak area from the Sample solution  
- \(r_L\) = peak area from the Standard solution  
- \(C_S\) = concentration of the Standard solution (mg/mL)  
- \(C_L\) = label claim (mg/Tablet)  
- \(V\) = volume of Medium, 900 mL  

**Correction factor = \((v \times P_L) / V\)**  
- \(v\) = volume of solution under test withdrawn (mL)  
- \(P_L\) = percentage of mycophenolate dissolved at 5 min  

**Correction of the percentage dissolved at 15 min:**

\[
\text{Result} = \text{Correction factor} \times \frac{P_L}{100}
\]

**Tolerances:** NLT 60% (Q) of the labeled amount of mycophenolate mofetil \((C_{23}H_{31}NO_{7})\) is dissolved in 5 min, and NLT 80% of the labeled amount of mycophenolate mofetil \((C_{23}H_{31}NO_{7})\) is dissolved in 15 min.  

**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  
**Times:** 5 and 15 min  
**Standard solution:** 0.011 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. Dilute 2 mL of the filtrate with Medium to 100 mL.  
**Detector:** UV 250 nm  
**Path length:** 1 cm  
**Blank:** Medium  

**Analysis:** Calculate the percentage of mycophenolate mofetil \((C_{23}H_{31}NO_{7})\) dissolved:

\[
\text{Result} = \left( \frac{A_0}{A_L} \right) \times \left( \frac{C_S}{C_L} \right) \times V \times 100
\]

where:
- \(A_0\) = absorbance of the Sample solution  
- \(A_L\) = absorbance of the Standard solution  
- \(C_S\) = concentration of the Standard solution (mg/mL)  
- \(C_L\) = label claim (mg/Tablet)  
- \(V\) = volume of Medium, 900 mL  

**Correction factor = \((v \times P_L) / V\)**  
- \(v\) = volume of solution under test withdrawn (mL)  
- \(P_L\) = percentage of mycophenolate dissolved at 5 min  

**Correction of the percentage dissolved at 15 min:**

\[
\text{Result} = \text{Correction factor} \times \frac{P_L}{100}
\]

**Tolerances:** NLT 70% (Q) of the labeled amount of mycophenolate mofetil \((C_{23}H_{31}NO_{7})\) is dissolved in 5 min, and NLT 85% of the labeled amount of mycophenolate mofetil \((C_{23}H_{31}NO_{7})\) is dissolved in 15 min.  

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

**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**  
**Samples:** Standard solution and Sample solution  

[NOTE—The run time for the Sample solution is three times that of the retention time of the mycophenolate mofetil peak.]

Calculate the percentage of each impurity in the portion of Tablets taken:

\[
\text{Result} = \left( \frac{r_0}{r_U} \right) \times \left( \frac{C_S}{C_U} \right) \times (1/\bar{F}) \times 100
\]

where:
- \(r_0\) = peak response of each individual impurity from the Sample solution  
- \(r_U\) = peak response of mycophenolate mofetil from the Sample 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)  
- \(\bar{F}\) = relative response factor for each individual impurity (see Table I)  

**Acceptance criteria:** See Table I. [NOTE—Disregard peaks at relative retention times of 1.45 and 2.15. Disregard any peaks less than 0.05%.]  

**Table I**

<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>NMT 1.0 (Feb 1, 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>1.0</td>
<td>NMT 2.0 (Feb 1, 2011)</td>
</tr>
<tr>
<td>Any single unspecified impurity</td>
<td></td>
<td>1.0</td>
<td>0.1 (Feb 1, 2011)</td>
</tr>
<tr>
<td>Total degradation products</td>
<td></td>
<td>1.5</td>
<td></td>
</tr>
</tbody>
</table>

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

©2011 The United States Pharmacopeial Convention All Rights Reserved.
methoxy-7-methyl-3-oxo-5-phthalanyl)-4-methyl-4-hexenoate.]

**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:** Place Tablets, equivalent to 2.5 g of mycophenolate mofetil based on the label claim, into a 1000-mL volumetric flask. Add 100 mL of water and shake mechanically for a minimum of 15 min. Add 700 mL of acetonitrile, sonicate for 15 min, and shake mechanically for 20 min. Dilute with acetonitrile to volume. Pass through a 0.45-µm pore size nylon filter, and discard the first 2 mL of 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°

**Flow rate:** 1.5 mL/min

**Run time:** 1.7 times the retention time of the mycophenolate mofetil peak

**Injection size:** 10 µL

**System suitability**

**Samples:** Standard solution and Sensitivity solution

[NOTE—The relative retention times for mycophenolate mofetil and mycophenolate Z-mycophenolate mofetil are 3.0 and 1.1, respectively.]

**Suitability requirements**

**Signal-to-noise ratio:** NLT 10, Sensitivity solution

**Tailing factor:** NMT 2.0, Standard solution

**Relative standard deviation:** NMT 5.0%, Standard solution

**Analysis**

**Samples:** Standard solution and Sample solution

Calculate the percentage of Z-mycophenolate mofetil 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 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 Dissolution test used only if Test 1 is not used.

**USP Reference Standards (11)**

USP Mycophenolate Mofetil RS \( \text{RS}^{2S} \) (USP33)

©2011 The United States Pharmacopeial Convention  All Rights Reserved.