Add the following:

■Mycophenolate Mofetil Tablets

DEFINITION

Mycophenolate Mofetil Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of mycophenolate mofetil ($C_{23}H_{31}NO_7$).

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: 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: 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 nylon 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 ($C_{23}H_{31}NO_7$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*
r_S = peak response 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: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **DISSOLUTION** ⟨711⟩

●**Test 1**● (RB 1-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 ($C_{23}H_{31}NO_7$) dissolved:

$$(A_U/A_S) \times (C_S/L) \times V \times 100$$

A_U = absorbance of the *Sample solution*
A_S = absorbance of the *Standard solution*
C_S = concentration of the *Standard solution* (mg/mL)
L = label claim (mg/Tablet)
V = volume of *Medium*, 900 mL

●Correction factor = $(v \times P_S)/V$

v = volume of solution under test withdrawn (mL)
P_S = percentage of mycophenolate dissolved at 5 min

Correction of the percentage dissolved at 15 min:

Result = Correction factor + percentage dissolved at 15 min

● (RB 1-Feb-2011)

Tolerances: NLT 75% (*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.

●**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 tof 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*.)

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:

$$\text{Result} = (r_U/r_S) \times (C_S/L) \times V \times 100$$

r_U = peak area from the *Sample solution*
r_S = peak area from the *Standard solution*
C_S = concentration of the *Standard solution*
L = label claim (mg/Tablet)
V = volume of *Medium*, 900 mL

$$\text{Correction factor} = (v \times P_S)/V$$

v = volume of solution under test withdrawn (mL)
P_S = percentage of mycophenolate dissolved at 5 min

Correction of the percentage dissolved at 15 min:

$$\text{Result} = \text{Correction factor} + \text{percentage dissolved at 15 min}$$

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:

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times V \times 100$$

A_U = absorbance of the *Sample solution*
A_S = absorbance of the *Standard solution*
C_S = concentration of the *Standard solution* (mg/mL)
L = label claim (mg/Tablet)
V = volume of *Medium*, 900 mL

$$\text{Correction factor} = (v \times P_S)/V$$

v = volume of solution under test withdrawn (mL)
P_S = percentage of mycophenolate dissolved at 5 min

Correction of the percentage dissolved at 15 min:

$$\text{Result} = \text{Correction factor} + \text{percentage dissolved at 15 min}$$

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. ● (RB 1-Feb-2011)

• **UNIFORMITY OF DOSAGE UNITS ⟨905⟩:** Meet the requirements

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, *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:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

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*. [NOTE—Disregard peaks at relative retention times of 1.45 and 2.15. Disregard any peaks less than 0.05%.]

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Mycophenolic acid[a]	0.6	1.4	●1.0● (RB 1-Feb-2011)
Mycophenolate *N*-oxide analog[b]	0.8	1.0	0.2
Mycophenolate mofetil	1.0	—	—
Any single unspecified impurity	—	1.0	0.1
Total degradation products	—	—	●1.5● (RB 1-Feb-2011)

[a] (*E*)-6-(1,3-Dihydro-4-hydroxy-6-methoxy-7-methyl-3-oxo-5-isobenzofuranyl)-4-methyl-4-hexenoic acid.
[b] 2-Morpholinoethyl (*E*)-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-morpholinoethyl (*Z*)-6-(4-hydroxy-6-

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 1.0 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:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

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.● (RB 1-Feb-2011)

- **USP REFERENCE STANDARDS** ⟨11⟩

USP Mycophenolate Mofetil RS■2S (*USP33*)