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Mycophenolate Mofetil Tablets

DEFINITION
Mycophenolate Mofetil Tablets contain NLT 94.0% and NMT 105.0% of the labeled amount of mycophenolate mofetil ($C_{23}H_{31}NO_7$).

IDENTIFICATION

Change to read:

• **A.** ▲The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-Aug-2023)

• **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**

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* (55:45)

Standard solution: 0.125 mg/mL of USP Mycophenolate Mofetil RS in acetonitrile

▲**Sample stock solution:** Nominally 2.5 mg/mL of mycophenolate mofetil prepared as follows. Transfer Tablets, equivalent to 2.5 g of mycophenolate mofetil, to 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.▲ (USP 1-Aug-2023)

Sample solution: ▲Nominally 0.125 mg/mL of mycophenolate mofetil in acetonitrile from *Sample stock solution*. Pass through a nylon filter of 0.45-µm pore size and discard the first 5 mL of the filtrate.▲ (USP 1-Aug-2023)

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

Mode: LC

Detector: UV 250 nm. ▲For *Identification A*, use a diode array detector in the range of 200–400 nm.▲ (USP 1-Aug-2023)

Column: 4.6-mm × 25-cm; 5-µm packing L7

Temperatures

Column: 45°

Autosampler: 10 ± 5°

Flow rate: 1.5 mL/min

Injection volume: 20 µL

▲**Run time:** NLT 3 times the retention time of mycophenolate mofetil peak▲ (USP 1-Aug-2023)

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 the labeled amount 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 of 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: 94.0%–105.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Test 1

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 filter of 0.45-µm pore size.

Instrumental conditions

▲(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)▲ (USP 1-Aug-2023)

Mode: UV

Analytical wavelength: 304 nm

Path length: 0.1 cm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of mycophenolate mofetil ($C_{23}H_{31}NO_7$) dissolved at each time point (*i*):

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

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of USP Mycophenolate Mofetil RS in the *Standard solution* (mg/mL)

Calculate the percentage of the labeled amount of mycophenolate mofetil ($C_{23}H_{31}NO_7$) dissolved at each time point (*i*):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

C_i = concentration of mycophenolate mofetil in the portion of sample withdrawn at the specified time (mg/mL)

V = volume of the *Medium*, 900 mL

L = label claim (mg/Tablet)

V_S = volume of the *Sample solution* withdrawn at each time point (mL)

Tolerances: See *Table 1*.

Table 1

Time Point (*i*)	Time (min)	Tolerances (*Q*)
1	5	NLT 75%
2	15	NLT 85%

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: 0.11 mg/mL of USP Mycophenolate Mofetil RS in *Diluent* from the *Standard stock solution*

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 volume: 20 µL

▲**Run time:** NLT 2.5 times the retention time of mycophenolate mofetil peak▲ (USP 1-Aug-2023)

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of mycophenolate mofetil ($C_{23}H_{31}NO_7$) dissolved at each time point (*i*):

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

r_U = peak response of 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)

D = dilution factor of the *Sample solution*, 5

Calculate the percentage of the labeled amount of mycophenolate mofetil ($C_{23}H_{31}NO_7$) dissolved at each time point (*i*):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

C_i = concentration of mycophenolate mofetil in the portion of sample withdrawn at the specified time (mg/mL)

V = volume of the *Medium*, 900 mL

L = label claim (mg/Tablet)

V_S = volume of the *Sample solution* withdrawn at each time point (mL)

Tolerances: See *Table 2*.

Table 2

Time Point (*i*)	Time (min)	Tolerances (*Q*)
1	5	NLT 60%
2	15	NLT 80%

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.

Instrumental conditions

▲(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)▲ (USP 1-Aug-2023)

Mode: UV

Analytical wavelength: 250 nm

Path length: 1 cm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of mycophenolate mofetil ($C_{23}H_{31}NO_7$) dissolved at each time point (*i*):

$$\text{Result} = (A_U/A_S) \times C_S \times D$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of USP Mycophenolate Mofetil RS in the *Standard solution* (mg/mL)

D = dilution factor of the *Sample solution*, 50

Calculate the percentage of the labeled amount of mycophenolate mofetil ($C_{23}H_{31}NO_7$) dissolved at each time point (*i*):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

C_i = concentration of mycophenolate mofetil in the portion of sample withdrawn at the specified time (mg/mL)

V = volume of the *Medium*, 900 mL

L = label claim (mg/Tablet)

V_S = volume of the *Sample solution* withdrawn at each time point (mL)

Tolerances: See *Table 3*.

Table 3

Time Point (*i*)	Time (min)	Tolerances (*Q*)
1	5	NLT 70%
2	15	NLT 85%

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

Change to read:

• **▲Organic Impurities▲** (USP 1-Aug-2023)

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▲from *Standard solution*▲ (USP 1-Aug-2023) in acetonitrile

System suitability

Samples: *Standard solution* and *Sensitivity solution*

Suitability requirements

Tailing factor: NMT 2, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

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

Analysis

▲▲ (USP 1-Aug-2023)

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ▲any specified and unspecified degradation product▲ (USP 1-Aug-2023) 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 ▲▲ (USP 1-Aug-2023) 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 ▲▲ (USP 1-Aug-2023) (see *Table 4*)

Acceptance criteria: See *Table 4*. ▲The reporting threshold is 0.05%.▲ (USP 1-Aug-2023)

Table 4

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Mycophenolic acid[a]	0.6	1.4	1.0
▲▲ (USP 1-Aug-2023) *N*-oxide analog[b]	0.8	1.0	0.2
Mycophenolate mofetil	1.0	—	—
▲Any unspecified degradation product▲ (USP 1-Aug-2023)	—	1.0	0.1
Total degradation products	—	—	1.5

[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.

Change to read:

• **Limit of *Z*-Mycophenolate Mofetil**

[Note—*Z*-Mycophenolate mofetil is ▲2-Morpholinoethyl (*Z*)-6-(1,3-dihydro-4-hydroxy-6-methoxy-7-methyl-3-oxo-5-isobenzofuranyl)-4-methyl-4-hexenoate.▲ (USP 1-Aug-2023)]

Triethylamine solution: Proceed as directed in the *Assay*.

Mobile phase: Acetonitrile and *Triethylamine solution* (35:65)

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

Sensitivity solution: 1.25 µg/mL of USP Mycophenolate Mofetil RS▲from *Standard solution*▲ (USP 1-Aug-2023) in acetonitrile

Sample solution: Nominally 2.5 mg/mL of mycophenolate mofetil prepared as follows. Transfer Tablets, equivalent to 2.5 g of mycophenolate mofetil, to 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 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°

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*

[Note—The relative retention times for mycophenolate mofetil and *Z*-mycophenolate mofetil are 1.0 and 1.1, respectively.]

Suitability requirements

Tailing factor: NMT 2.0, *Standard solution*

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

Signal-to-noise ratio: NLT 10, *Sensitivity 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: NMT 0.10%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed, light-resistant 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 Mycophenolate Mofetil RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
MYCOPHENOLATE MOFETIL TABLETS	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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