Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-Dec-2017
Document Type: USP Monographs
DocId: GUID-515D0785-A0CE-462F-A2E0-7C3820E630E7_4_en-US
DOI: https://doi.org/10.31003/USPNF_M5367_04_01
DOI Ref: fj5h9

Mycophenolic Acid Delayed-Release Tablets

DEFINITION

Mycophenolic Acid Delayed-Release Tablets contain an amount of mycophenolate sodium equivalent to NLT 95.0% and NMT 105.0% of the labeled amount of mycophenolic acid ($C_{17}H_{20}O_6$).

IDENTIFICATION

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

ASSAY

- **Procedure**

Protect solutions from light.

Solution A: Dissolve 21 g of citric acid in a suitable volume of water, add 200 mL of 1 M sodium hydroxide solution, and dilute with water to 1 L.

Buffer: *Solution A* and 0.1 M hydrochloric acid (399:601)

Solution B: Acetonitrile, *Buffer*, and water (40:15:45)

Solution C: Acetonitrile and *Buffer* (85:15)

Mobile phase: See *Table 1*. Return to original conditions, and re-equilibrate the system.

Table 1

Time (min)	Solution B (%)	Solution C (%)
0	100	0
9	100	0
18	0	100
22	0	100

Diluent: *Solution B*

Standard solution: 0.385 mg/mL of USP Mycophenolate Sodium RS in *Diluent*. Stir magnetically for at least 60 min to aid dissolution.

Sample stock solution: Nominally equivalent to 9 mg/mL of mycophenolic acid in *Diluent* prepared as follows. Transfer NLT 25 Tablets to a volumetric flask and add *Diluent* to volume. Add a stirring bar and stir vigorously for at least 60 min. Centrifuge a portion of the suspension and use the clear supernatant.

Sample solution: Nominally equivalent to 0.36 mg/mL of mycophenolic acid in *Diluent* from *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 251 nm or diode array. [Note—Use a diode array detector to perform *Identification B*.]

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

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of mycophenolic acid ($C_{17}H_{20}O_6$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of mycophenolate from the *Sample solution*

r_S = peak response of mycophenolate from the *Standard solution*

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

C_U = nominal concentration of mycophenolic acid in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of mycophenolic acid, 320.34

M_{r2} = molecular weight of mycophenolate sodium, 342.32

Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Protect solutions from light.

Acid stage

Acid stage medium: 0.1 N hydrochloric acid; 750 mL

Apparatus 2: 50 rpm

Time: 2 h

Determine the percentage of the labeled amount of mycophenolic acid ($C_{17}H_{20}O_6$) dissolved by using one of the following procedures.

Spectrophotometric procedure

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Standard solution: Transfer USP Mycophenolate Sodium RS to a suitable volumetric flask, dissolve in methanol equivalent to 5% of the final volume, and dilute with *Acid stage medium* to volume to obtain the solution having the following concentrations:

For Tablets labeled to contain 180 mg of mycophenolic acid: 0.0128 mg/mL of USP Mycophenolate Sodium RS

For Tablets labeled to contain 360 mg of mycophenolic acid: 0.0256 mg/mL of USP Mycophenolate Sodium RS

Sample solution: Centrifuge portions of the solution under test or pass through a suitable glass fiber filter of 1-µm pore size.

Instrumental conditions

Mode: UV

Analytical wavelength: 250 nm

Cell path length

For Tablets containing 180 mg of mycophenolic acid per Tablet: 0.2 cm

For Tablets containing 360 mg of mycophenolic acid per Tablet: 0.1 cm

Blank: *Acid stage medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of mycophenolic acid ($C_{17}H_{20}O_6$) dissolved:

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times V \times (M_{r1}/M_{r2}) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

L = label claim (mg/Tablet)

V = volume of *Acid stage medium*, 750 mL

M_{r1} = molecular weight of mycophenolic acid, 320.34

M_{r2} = molecular weight of mycophenolate sodium, 342.32

Chromatographic procedure

Solution A: Solution of 4 mL of triethylamine in 1300 mL of water. Adjust with phosphoric acid to a pH of 5.3.

Mobile phase: Acetonitrile and *Solution A* (35:65)

Diluent: Mixture of 0.1 N hydrochloric acid and 0.2 M sodium phosphate (75:25), adjusted with either 2 M sodium hydroxide or hydrochloric acid to a pH of 6.8

Standard solution: Solution of USP Mycophenolate Sodium RS in *Diluent*, equivalent to (L/1000) mg/mL of mycophenolic acid, where L is the label claim in mg/Tablet

Sample solution: Mix 10 mL of the solution under test and 10 mL of 0.2 M sodium phosphate.

Chromatographic system

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

Mode: LC

Detector: UV 250 nm

Column: 4.6-mm × 25-cm; 5-µm packing L11

Temperatures

Autosampler: 4°

Column: 45°

Flow rate: 1.5 mL/min

Injection volume: 5 µL

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 percentage of the labeled amount of mycophenolic acid ($C_{17}H_{20}O_6$) dissolved:

$$(r_U/r_S) \times (C_S/L) \times V \times D \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

L = label claim (mg/Tablet)

V = volume of *Acid stage medium*, 750 mL

D = dilution factor for the *Sample solution*

M_{r1} = molecular weight of mycophenolic acid, 320.34

M_{r2} = molecular weight of mycophenolate sodium, 342.32

Tolerances: NMT 5% of the labeled amount of mycophenolic acid ($C_{17}H_{20}O_6$) is dissolved.

Buffer stage

Buffer stage medium: After 2 h, continue with a pH 6.8 phosphate buffer as follows. Add 250 mL of 0.2 M sodium phosphate and adjust, if necessary, with 2 M sodium hydroxide or hydrochloric acid to a pH of 6.8; 1000 mL. [NOTE—If the volume of the sample withdrawn is greater than 2 mL, replace it with *Acid stage medium*. Alternatively, increase the volume of 0.2 M sodium phosphate being added to obtain the final volume of 1000 mL and adjust, if necessary, with 2 M sodium hydroxide or hydrochloric acid to a pH of 6.8.]

Apparatus 2: 50 rpm

Time: 1 h. [NOTE—The total time for this analysis is 3 h, where 2 h is from the *Acid stage* and 1 h is from the *Buffer stage*.]

Determine the percentage of the labeled amount of mycophenolic acid ($C_{17}H_{20}O_6$) dissolved by using one of the following procedures.

Spectrophotometric procedure

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Standard solution: Solution of USP Mycophenolate Sodium RS, equivalent to (*L*/1000) mg/mL of mycophenolic acid, where *L* is the label claim, in mg/Tablet. Prepare the solution as follows. Transfer USP Mycophenolate Sodium RS to a suitable volumetric flask, dissolve in methanol equivalent to 5% of the final volume, and dilute with *Buffer stage medium* to volume.

Sample solution: Centrifuge portions of the solution under test or pass through a suitable glass fiber filter of 1-µm pore size.

Instrumental conditions

Mode: UV

Analytical wavelength: 250 nm

Cell path length

For Tablets containing 180 mg of mycophenolic acid per Tablet: 0.2 cm

For Tablets containing 360 mg of mycophenolic acid per Tablet: 0.1 cm

Blank: *Buffer stage medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of mycophenolic acid ($C_{17}H_{20}O_6$) dissolved:

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times V \times (M_{r1}/M_{r2}) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

L = label claim (mg/Tablet)

V = volume of *Buffer stage medium*, 1000 mL

M_{r1} = molecular weight of mycophenolic acid, 320.34

M_{r2} = molecular weight of mycophenolate sodium, 342.32

Chromatographic procedure

Solution A, Mobile phase, Standard solution, and **Chromatographic system:** Proceed as directed under *Chromatographic procedure* in *Acid stage*.

Sample solution: Pass the solution under test through a suitable polyethersulfone membrane filter of 0.45-µm pore size and discard a few milliliters of the filtrate.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of mycophenolic acid ($C_{17}H_{20}O_6$) dissolved:

$$(r_U/r_S) \times (C_S/L) \times V \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

L = label claim (mg/Tablet)

V = volume of *Buffer stage medium*, 1000 mL

M_{r1} = molecular weight of mycophenolic acid, 320.34

M_{r2} = molecular weight of mycophenolate sodium, 342.32

Tolerances: NLT 80% (*Q*) of the labeled amount of mycophenolic acid ($C_{17}H_{20}O_6$) is dissolved.

- **Uniformity of Dosage Units** ⟨905⟩, *Weight Variation*: Meet the requirements

IMPURITIES

• Organic Impurities

Protect solutions from light.

Mobile phase, Diluent, Standard solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability solution: 0.36 µg/mL of USP Mycophenolate Mofetil Related Compound B RS and 0.385 mg/mL of USP Mycophenolate Sodium RS in *Diluent*. Stir magnetically for at least 60 min to aid dissolution.

Sensitivity solution: 0.18 µg/mL of USP Mycophenolate Sodium RS in *Diluent* from *Standard solution*

System suitability

Samples: *Standard solution*, *System suitability solution*, and *Sensitivity solution*

Suitability requirements

Resolution: NLT 1.5 between the mycophenolate mofetil related compound B and mycophenolate peaks, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

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

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

Analysis

Samples: *Standard solution* and *Sample solution*

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

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of each individual impurity from the *Sample solution*

r_S = peak response of mycophenolate from the *Standard solution*

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

C_U = nominal concentration of mycophenolic acid in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of mycophenolic acid, 320.34

M_{r2} = molecular weight of mycophenolate sodium, 342.32

Acceptance criteria: See *Table 2*. The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Phthalic acid[a]	0.30	—
Phthalic acid monoethyl ester[a,b]	0.55	—
Mycophenolate mofetil related compound B	0.90	0.2
Mycophenolate	1.0	—
Ethyl ester of mycophenolate[c]	2.3	0.2
Any individual unspecified impurity	—	0.1
Total impurities	—	1.0

[a] It is a process impurity and is listed for identification only. It is controlled in the drug substance. It is not reported for the drug product and should not be included in the total impurities.

[b] 2-(Ethoxycarbonyl)benzoic acid.

[c] Ethyl (*E*)-6-(4-hydroxy-6-methoxy-7-methyl-3-oxo-1,3-dihydroisobenzofuran-5-yl)-4-methylhex-4-enoate.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and protect from moisture. Store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Mycophenolate Mofetil Related Compound B RS

(*RS*)-7-Hydroxy-5-methoxy-4-methyl-6-[2-(5-methyl-2-oxo-tetrahydrofuran-5-yl)ethyl]-3*H*-isobenzofuran-1-one.

$C_{17}H_{20}O_6$ 320.34

USP Mycophenolate Sodium RS

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

Topic/Question	Contact	Expert Committee
MYCOPHENOLIC ACID DELAYED-RELEASE TABLETS	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 43(1)

Current DocID: GUID-515D0785-A0CE-462F-A2E0-7C3820E630E7_4_en-US
Previous DocID: GUID-515D0785-A0CE-462F-A2E0-7C3820E630E7_2_en-US
DOI: https://doi.org/10.31003/USPNF_M5367_04_01
DOI ref: fj5h9