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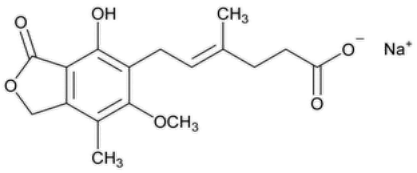
Mycophenolate Sodium



$C_{17}H_{19}NaO_6$ 342.32

4-Hexenoic acid, 6-(1,3-dihydro-4-hydroxy-6-methoxy-7-methyl-3-oxo-5-isobenzofuranyl)-4-methyl-, monosodium salt, (*E*)-;

Sodium (*E*)-6-(4-hydroxy-6-methoxy-7-methyl-3-oxo-1,3-dihydroisobenzofuran-5-yl)-4-methylhex-4-enoate CAS RN®: 37415-62-6.

DEFINITION

Mycophenolate Sodium contains NLT 98.0% and NMT 102.0% of mycophenolate sodium ($C_{17}H_{19}NaO_6$), calculated on the anhydrous basis.

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A, 197K, or 197M
- **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**

Protect solutions from light.

Solution A: Acetonitrile, phosphoric acid, and water (100:0.2:900)

Solution B: Acetonitrile, phosphoric acid, and water (800:0.2:200)

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

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
35	10	90
40	10	90

Diluent: Methanol and water (1:9)

Standard solution: 0.08 mg/mL of USP Mycophenolate Sodium RS in *Diluent*. Protect from light.

Sample solution: 0.08 mg/mL of Mycophenolate Sodium in *Diluent*. Protect from light.

Chromatographic system

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

Mode: LC

Detector: UV 216 nm

Column: 3-mm × 25-cm; 5-µm packing L1

Column temperature: 50°

Flow rate: 0.8 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 0.73%

Tailing factor: 0.7–1.5

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of mycophenolate sodium ($C_{17}H_{19}NaO_6$) in the portion of Mycophenolate Sodium 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 Sodium RS in the *Standard solution* (mg/mL)

C_U = concentration of Mycophenolate Sodium in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

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 stock solution 1: 0.02 mg/mL of USP Mycophenolate Mofetil Related Compound B RS prepared as follows. Transfer USP Mycophenolate Mofetil Related Compound B RS to a suitable volumetric flask and dilute in methanol equivalent to 10% of the final volume, and then dilute with water to volume.

System suitability stock solution 2: Transfer 4.0 mL of *System suitability stock solution 1* to a 100-mL volumetric flask and dilute with *Diluent* to volume.

System suitability solution: 0.8 µg/mL of USP Mycophenolate Mofetil Related Compound B RS and 0.08 mg/mL of USP Mycophenolate Sodium RS prepared by dissolving a suitable amount of USP Mycophenolate Sodium RS in *System suitability stock solution 2*

Sensitivity solution: 0.024 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*

Relative standard deviation: NMT 0.73%, *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 Mycophenolate Sodium taken:

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

r_U = peak response of each 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 = concentration of Mycophenolate Sodium in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 2*. Disregard any impurity peak less than 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Mycophenolate mofetil related compound B[a]	0.9	0.1
Mycophenolate	1.0	—
Any individual unspecified impurity	—	0.07
Total impurities	—	0.4

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

SPECIFIC TESTS

• **Sodium Content**

Standard stock solution: Use commercially available sodium atomic absorption spectroscopy standard solution of 1000 µg/mL of sodium in 0.5 M nitric acid.

Diluent: Transfer 3 mL of nitric acid to a 250-mL volumetric flask, and dilute with water to volume.

Standard solution A: 6.0 µg/mL of sodium in *Diluent* from *Standard stock solution*

Standard solution B: 9.0 µg/mL of sodium in *Diluent* from *Standard stock solution*

Standard solution C: 12.0 µg/mL of sodium in *Diluent* from *Standard stock solution*

Sample solution: 0.14 mg/mL of Mycophenolate Sodium prepared as follows. Weigh 30–40 mg of Mycophenolate Sodium into a digestion vessel, add 3 mL of nitric acid and digest at 150° for 5 h. Allow to cool, transfer the digestion solution to a 250-mL volumetric flask, and dilute with water to volume.

Instrumental conditions

(See *Atomic Absorption Spectroscopy* ⟨852⟩.)

Mode: Atomic absorption spectrophotometry

Analytical wavelength: 589.0 nm

Lamp: Sodium hollow-cathode

Flame: Air–acetylene

Blank: *Diluent*

System suitability

Sample: *Standard solution B*

Suitability requirements

Relative standard deviation: NMT 5% for absorbance from three readings

Analysis

Samples: *Standard solutions*, *Sample solution*, and *Blank*

Plot the absorbances of the *Blank* and *Standard solutions* versus their concentrations of sodium (0, 6.0, 9.0, and 12.0 µg/mL), and draw a calibration curve best fitting the four points. From the graph so obtained, determine the concentration, in µg/mL, of sodium in the *Sample solution*.

Calculate the percentage of sodium in the portion of Mycophenolate Sodium taken:

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

F = conversion factor (0.001 mg/µg)

C_S = concentration of sodium in the *Sample solution* (µg/mL)

C_U = concentration of Mycophenolate Sodium in the *Sample solution* (mg/mL)

Acceptance criteria: 5.7%–7.7% on the anhydrous basis

Change to read:

• **▲X-Ray Powder Diffraction ⟨941⟩▲** (CN 1-May-2022)**:** Its X-ray diffraction pattern conforms to that of USP Mycophenolate Sodium RS, similarly determined.

• **Water Determination, *Method Ia*⟨921⟩:** NMT 1.5%

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** The total aerobic microbial limit does not exceed 10^3 cfu/g. The total yeasts and molds count does not exceed 10^2 cfu/g.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers. Protect from light.

• **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
MYCOPHENOLATE SODIUM	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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