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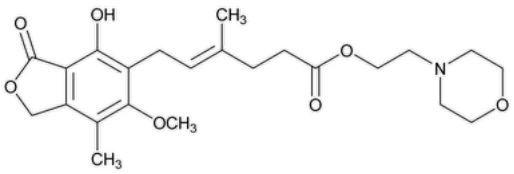
Mycophenolate Mofetil



$C_{23}H_{31}NO_7$ 433.49

4-Hexenoic acid, 6-(1,3-dihydro-4-hydroxy-6-methoxy-7-methyl-3-oxo-5-isobenzofuranyl)-4-methyl-, 2-(4-morpholinyl)ethyl ester, (*E*)-;

2-Morpholinoethyl (*E*)-6-(4-hydroxy-6-methoxy-7-methyl-3-oxo-5-phthalanyl)-4-methyl-4-hexenoate CAS RN®: 128794-94-5; UNII: 9242ECW6R0.

DEFINITION

Mycophenolate Mofetil contains NLT 98.0% and NMT 102.0% of mycophenolate mofetil ($C_{23}H_{31}NO_7$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)

• **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**

Buffer: Triethylamine and water (1:325). Adjust with phosphoric acid to a pH of 5.3.

Mobile phase: Acetonitrile and *Buffer* (7:13)

Standard solution: 0.4 mg/mL of USP Mycophenolate Mofetil RS in acetonitrile

Sample solution: 0.4 mg/mL of Mycophenolate Mofetil in acetonitrile

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°

Flow rate: 1.5 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 mycophenolate mofetil ($C_{23}H_{31}NO_7$) in the portion of Mycophenolate Mofetil 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 = concentration of Mycophenolate Mofetil in the *Sample solution* (mg/mL)

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

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

• **Organic Impurities**

Buffer and **Mobile phase:** Prepare as directed in the *Assay*.

Sample solution: 2 mg/mL of Mycophenolate Mofetil in acetonitrile

System suitability solution: 10 µg/mL each of USP Mycophenolate Mofetil Related Compound A RS and USP Mycophenolate Mofetil Related Compound B RS in acetonitrile

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°

Flow rate: 1.5 mL/min

Injection volume: 10 µL

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 1.5 between mycophenolate mofetil related compound A and mycophenolate mofetil related compound B

Analysis

Sample: *Sample solution*

Calculate the percentage of each impurity in the portion of Mycophenolate Mofetil taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response for each impurity

r_T = sum of all the peak responses

Acceptance criteria: See *Table 1*. Disregard any peak less than 0.03%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Mycophenolic acid[a]	0.33	0.50
Mycophenolate mofetil related compound A[b]	0.45	0.10
Mycophenolate mofetil related compound B[c]	0.49	0.10
N-Oxide analog[d]	0.60	0.10
1-Morpholinoethoxy analog[e]	0.86	0.10
Mycophenolate mofetil	1.0	—
Z-Mycophenolate mofetil[f]	1.1	0.10
O-Methyl analog[g]	1.2	0.10
Methyl mycophenolate[h]	1.5	0.10
Any single unspecified impurity	—	0.10
Total impurities	—	0.70

[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-4,6-dihydroxy-7-methyl-3-oxo-5-isobenzofuranyl)-4-methyl-4-hexenoate.

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

[d] 2-Morpholinoethyl (*E*)-6-(1,3-dihydro-4-hydroxy-6-methoxy-7-methyl-3-oxo-5-isobenzofuranyl)-4-methyl-4-hexenoate *N*-oxide.

[e] 2-Morpholinoethyl (*RS*)-(*E*)-6-(1,3-dihydro-4-hydroxy-6-methoxy-7-methyl-1-(2-morpholinoethoxy)-3-oxo-5-isobenzofuranyl)-4-methyl-4-hexenoate.

[f] 2-Morpholinoethyl (*Z*)-6-(1,3-dihydro-4-hydroxy-6-methoxy-7-methyl-3-oxo-5-isobenzofuranyl)-4-methyl-4-hexenoate.

[g] 2-Morpholinoethyl (*E*)-6-(1,3-dihydro-4,6-dimethoxy-7-methyl-3-oxo-5-isobenzofuranyl)-4-methyl-4-hexenoate.

[h] Methyl (*E*)-6-(1,3-dihydro-4-hydroxy-6-methoxy-7-methyl-3-oxo-5-isobenzofuranyl)-4-methyl-4-hexenoate.

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

Analysis: Dry a sample under vacuum at 60° for 3 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store at room temperature.

• **USP Reference Standards** ⟨11⟩

USP Mycophenolate Mofetil RS

USP Mycophenolate Mofetil Related Compound A RS

2-Morpholinoethyl (*E*)-6-(1,3-dihydro-4,6-dihydroxy-7-methyl-3-oxo-5-isobenzofuranyl)-4-methyl-4-hexenoate.

$C_{22}H_{29}NO_7$ 419.47

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

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

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

Chromatographic Database Information: Chromatographic Database

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