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Mycophenolate Mofetil for Injection

DEFINITION

Mycophenolate Mofetil for Injection contains an amount of Mycophenolate Mofetil Hydrochloride equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of mycophenolate mofetil ($C_{23}H_{31}NO_7$).

IDENTIFICATION

Change to read:

• **▲A.▲** (USP 1-MAY-2019) The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

Add the following:

▲• B. 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-May-2019)

ASSAY

Change to read:

• **PROCEDURE**

Protect solutions from light.

Buffer 1: Transfer 10 mL of triethylamine to a 1000-mL volumetric flask containing about 950 mL of water and mix. Adjust with phosphoric acid to a pH of 7.2, and dilute with water to volume.

Buffer 2: Transfer 10 mL of triethylamine to a 1000-mL volumetric flask containing about 950 mL of water and mix. Adjust with phosphoric acid to a pH of 3.0, and dilute with water to volume.

Solution A: *Buffer 1* and water (4:9)

Diluent: Acetonitrile, *Buffer 2*, and water (7:4:9)

Mobile phase: Acetonitrile and *Solution A* (3:7)

Standard stock solution: 1.0 mg/mL of USP Mycophenolate Mofetil RS in *Diluent* prepared as follows. Transfer a known quantity of USP Mycophenolate Mofetil RS to a suitable volumetric flask, add acetonitrile equivalent to about 10% of the final volume, sonicate for about 5 min or until the solid dissolves, and dilute with *Diluent* to volume.

Standard solution: 0.4 mg/mL of USP Mycophenolate Mofetil RS in *Diluent* from *Standard stock solution*

Sample stock solution: Nominally equivalent to 10 mg/mL of mycophenolate mofetil prepared as follows. Constitute each of the containers of Mycophenolate Mofetil for Injection with 14 mL of 5% dextrose injection. Quantitatively transfer the contents of all vials, the combined contents of which are equivalent to about 2 g of mycophenolate mofetil, to a 200-mL volumetric flask, and dilute with water to volume.

Sample solution: Nominally equivalent to 0.4 mg/mL of mycophenolate mofetil in *Diluent* from *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 249 nm. ▲For *Identification B*, use a diode array detector in the range of 200–400 nm.▲ (USP 1-May-2019)

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

Temperatures

Autosampler: 5°

Column: 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 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 Mycophenolate Mofetil for Injection 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

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

IMPURITIES

Change to read:

• **Organic Impurities**

Protect solutions from light.

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

System suitability solution: 0.01 mg/mL of USP Mycophenolate Mofetil Related Compound A RS and 0.01 mg/mL of USP Mycophenolate Mofetil Related Compound B RS in *Diluent*

Sensitivity solution: 0.2 µg/mL in *Diluent* from the *Standard solution*

System suitability

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

[Note—The relative retention times for mycophenolate mofetil related compound A and mycophenolate mofetil related compound B are 0.40 and 0.46, respectively, measured with respect to mycophenolate mofetil.]

Suitability requirements

Resolution: NLT 2.0 between mycophenolate mofetil related compound A and mycophenolate mofetil related compound B, *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*

[Note—The run time for the *Sample solution* is NLT 1.5 times the retention time of the mycophenolate mofetil peak.]

Calculate the percentage of each impurity in the portion of Mycophenolate Mofetil for Injection 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 (see *Table 1*)

Acceptance criteria: See *Table 1*. ▲The reporting threshold is 0.05%.▲ (USP 1-May-2019)

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Mycophenolic acid[a]	0.12	1.4	1.1
Mycophenolate mofetil	1.00	—	—

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Any unspecified impurity	—	1.0	0.1
Total impurities	—	—	1.35

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

SPECIFIC TESTS

Change to read:

• **Bacterial Endotoxins Test** ⟨85⟩**:** ▲Meets the requirements▲ (USP 1-May-2019)

Change to read:

• **Sterility Tests** ⟨71⟩**:** Meets the requirements ▲▲ (USP 1-May-2019)

• **Water Determination** ⟨921⟩, *Method I, Method Ia***:** NMT 1.0%

• **pH** ⟨791⟩**:** 2.7–4.1, in a reconstituted solution

• **Particulate Matter in Injections** ⟨788⟩**:** Meets the requirements for small-volume injections

• **Constituted Solution:** At the time of use, meets the requirements in *Injections and Implanted Drug Products* ⟨1⟩, *Product Quality Tests Common to Parenteral Dosage Forms, Specific Tests, Completeness and Clarity of Solutions*

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers and store at controlled 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 FOR INJECTION	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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