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Imiquimod Cream

DEFINITION

Imiquimod Cream contains NLT 90% and NMT 110% of the labeled amount of imiquimod ($C_{14}H_{16}N_4$).

IDENTIFICATION

Change to read:

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

Wavelength range: 220–400 nm

Diluent: Acetonitrile and 0.1 N hydrochloric acid (30:70)

Standard solution: 2 µg/mL of USP Imiquimod RS in *Diluent*. Sonicate, if necessary, to dissolve.

Sample stock solution: Nominally 20 µg/mL of imiquimod in *Diluent* prepared as follows. Transfer a portion of Cream equivalent to 5 mg of imiquimod into a 250-mL volumetric flask. Add about 60% of the flask volume of *Diluent* and sonicate for 30 min with occasional swirling to dissolve, if necessary. Dilute with *Diluent* to volume.

Sample solution: Nominally 2 µg/mL of imiquimod from *Sample stock solution* in *Diluent*. Pass through a suitable filter.

Acceptance criteria: The UV absorption spectrum of the *Sample solution* exhibits maxima and minima at the same wavelengths as that of the *Standard solution*.

• **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: 1.17 g/L of sodium 1-octanesulfonate in water. Add 1 mL of triethylamine for each liter of solution and adjust with perchloric acid to a pH of 2.5.

Mobile phase: Acetonitrile and *Buffer* (270:730)

Diluent: Acetonitrile and 0.1 N hydrochloric acid (30:70)

Standard stock solution: 0.2 mg/mL of USP Imiquimod RS in *Diluent*. Sonicate to dissolve, if necessary.

Standard solution: 0.01 mg/mL of USP Imiquimod RS in *Mobile phase* from *Standard stock solution*

Sample stock solution: Nominally 0.2 mg/mL of imiquimod in *Diluent* prepared as follows. Transfer a portion of Cream equivalent to about 50 mg of imiquimod into a 250-mL volumetric flask. Add about 60% of the flask volume of *Diluent,* sonicate for 30 min with occasional swirling to dissolve, and cool if necessary. Dilute with *Diluent* to volume.

Sample solution: Nominally 0.01 mg/mL of imiquimod from *Sample stock solution* in *Mobile phase*. Pass through a suitable filter.

Chromatographic system

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

Mode: LC

Detector: UV 226 nm

Column: 4.6-mm × 15-cm; 5-µm packing L7

Column temperature: 30°

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 imiquimod ($C_{14}H_{16}N_4$) in the portion of Cream taken:

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

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

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

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

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

Acceptance criteria: 90%–110%

PERFORMANCE TESTS

• **Minimum Fill ⟨755⟩:** Meets the requirement

IMPURITIES

• **Organic Impurities**

Solution A: 1.17 g/L of sodium 1-octanesulfonate in water. Add 1 mL of triethylamine for each liter of solution and adjust with perchloric acid to a pH of 2.5.

Solution B: Acetonitrile and methanol (90:10)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
30	70	30
45	40	60
55	40	60
60	90	10
70	90	10

Diluent: Acetonitrile and 0.1 N hydrochloric acid (30:70)

Standard stock solution: 0.5 mg/mL of USP Imiquimod RS in *Diluent*. Sonicate to dissolve, if necessary.

Standard solution: 0.5 µg/mL of USP Imiquimod RS from *Standard stock solution* in *Diluent*

Sample solution: Nominally 0.5 mg/mL of imiquimod prepared as follows. Transfer a portion of Cream equivalent to 25 mg of imiquimod into a 50-mL volumetric flask. Add about 30 mL of *Diluent*, and sonicate for 40 min with occasional swirling. Dilute with *Diluent* to final volume. Pass through a suitable filter.

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 50°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Samples: *Standard stock solution* and *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0, *Standard stock solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Cream 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 imiquimod from the *Standard solution*

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

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

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*. Disregard any peak below 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Imiquimod related compound B[a]	0.57	1.15	0.2
Imiquimod related compound A[b]	0.77	1.5	—[c]
Imiquimod	1.0	—	—
Imiquimod related compound C[d]	1.2	1.85	—[c]
Any unspecified individual impurity	—	1.0	0.5
Total impurities	—	—	1.0

[a] 1-Isobutyl-1*H*-imidazo[4,5-*c*]quinoline 5-oxide.

[b] 1-Isobutyl-1*H*-imidazo[4,5-c]quinoline.

[c] Process impurities monitored in the drug substance and not included in the calculation of total impurities.

[d] 4-Chloro-1-isobutyl-1*H*-imidazo[4,5-*c*]quinoline.

SPECIFIC TESTS

• **pH** ⟨791⟩

Sample: Nominally 2.5 mg/mL of imiquimod from Cream in water. Sonicate to disperse with constant swirling.

Acceptance criteria: 4.5–7.0

• **Microbial Enumeration Tests** ⟨61⟩ and **Tests For Specified Microorganisms** ⟨62⟩**:** The total aerobic microbial count is NMT 10^2 cfu/g, and the total yeasts and molds count is NMT 10^1 cfu/g. It meets the requirements for absence of *S. aureus* and *P. aeruginosa*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store at 4°–25°. Protect from freezing.

• **USP Reference Standards** ⟨11⟩

USP Imiquimod RS

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

Topic/Question	Contact	Expert Committee
IMIQUIMOD CREAM	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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