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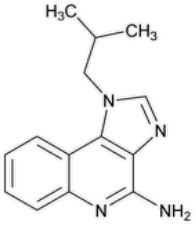
Imiquimod



$C_{14}H_{16}N_4$ 240.30

1*H*-Imidazo[4,5-c]quinolin-4-amine, 1-(2-methylpropyl)-;

4-Amino-1-isobutyl-1*H*-imidazo[4,5-c]quinoline CAS RN®: 99011-02-6; UNII: P1QW714R7M.

DEFINITION

Imiquimod contains NLT 98.0% and NMT 102.0% of imiquimod ($C_{14}H_{16}N_4$), 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: 0.005 M sodium 1-octanesulfonate in water containing 0.1% triethylamine. Adjust with dilute perchloric acid to a pH of 2.0.

Mobile phase: Acetonitrile and *Buffer* (27:73)

Standard solution: 50 µg/mL of USP Imiquimod RS in *Mobile phase*

Sample solution: 50 µg/mL of Imiquimod in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 226 nm

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

Flow rate: 1.5 mL/min

Injection volume: 20 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 imiquimod ($C_{14}H_{16}N_4$) in the portion of Imiquimod 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 Imiquimod RS in the *Standard solution* (µg/mL)

C_U = concentration of Imiquimod in the *Sample solution* (µg/mL)

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

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.2%
- **Organic Impurities**

Buffer: 0.005 M sodium octanesulfonate in water containing 0.1% triethylamine. Adjust with dilute perchloric acid to a pH of 2.0.

Diluent: Acetonitrile and *Buffer* (20:80)

Solution A: *Buffer*

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	80	20
20	80	20
45	10	90
50	10	90
55	80	20
65	80	20

Standard solution: 1.25 µg/mL each of USP Imiquimod Related Compound A RS, USP Imiquimod Related Compound B RS, USP Imiquimod Related Compound C RS, and USP Imiquimod RS in *Diluent*

Sample solution: 0.25 mg/mL of Imiquimod in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 226 nm

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

Column temperature: 45°

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 3 between imiquimod and imiquimod related compound C

Relative standard deviation: NMT 3.0% for imiquimod

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each known impurity in the portion of Imiquimod taken:

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

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

r_S = peak response of the corresponding related compound from the *Standard solution*

C_S = concentration of the corresponding Reference Standard in the *Standard solution* (µg/mL)

C_U = concentration of Imiquimod in the *Sample solution* (µg/mL)

Calculate the percentage of any other impurity in the portion of Imiquimod taken:

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

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* (µg/mL)

C_U = concentration of Imiquimod in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Imiquimod related compound B	0.30	0.15
Imiquimod related compound A	0.43	0.15
Imiquimod	1.0	—
Imiquimod related compound C	1.12	0.15
Any unspecified individual impurity	—	0.10
Total impurities	—	0.50

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

Analysis: Dry a sample at 100°–105° for 3 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

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

• **USP Reference Standards** ⟨11⟩

USP Imiquimod RS

USP Imiquimod Related Compound A RS

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

$C_{14}H_{15}N_3$ 225.29

USP Imiquimod Related Compound B RS

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

$C_{14}H_{15}N_3O$ 241.29

USP Imiquimod Related Compound C RS

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

$C_{14}H_{14}ClN_3$ 259.73

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. Information currently unavailable

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