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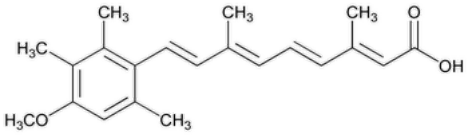
Acitretin



$C_{21}H_{26}O_3$ 326.43

2,4,6,8-Nonatetraenoic acid, 9-(4-methoxy-2,3,6-trimethylphenyl)-3,7-dimethyl-, (*all-E*)-;

(*all-E*)-9-(4-Methoxy-2,3,6-trimethylphenyl)-3,7-dimethyl-2,4,6,8-nonatetraenoic acid CAS RN®: 55079-83-9; UNII: LCH760E9T7.

DEFINITION

Acitretin contains NLT 98.0% and NMT 102.0% of $C_{21}H_{26}O_3$, calculated on the dried basis.

[CAUTION—Acitretin is a teratogen. Great care should be taken when handling to avoid inhalation of dust or contact with skin.]

[NOTE—Use low-actinic glassware and perform all tests under yellow and subdued light.]

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**

[NOTE—Store the solutions at 4° before injection.]

Mobile phase: Alcohol, glacial acetic acid, and water (92:0.3:8)

System suitability stock solution: 0.01 mg/mL each of USP Acitretin RS and USP Tretinoin RS in alcohol. [NOTE—Dissolve in tetrahydrofuran before diluting with alcohol.]

System suitability solution: 0.25 µg/mL each of USP Acitretin RS and USP Tretinoin RS in alcohol, from *System suitability stock solution*

Standard solution: 0.1 mg/mL of USP Acitretin RS in alcohol. [NOTE—Dissolve in tetrahydrofuran before diluting with alcohol. The final concentration of tetrahydrofuran in the preparation will be 2%.]

Sample stock solution: 0.25 mg/mL of Acitretin in tetrahydrofuran and alcohol (1:19). [NOTE—Dissolve in tetrahydrofuran before diluting with alcohol.]

Sample solution: 0.1 mg/mL of Acitretin in alcohol, from *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 360 nm

Column: 4-mm × 25-cm; packing L1

Flow rate: 0.6 mL/min

Injection size: 10 µL

System suitability

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

[NOTE—The relative retention times for tretinoin and acitretin are 0.84 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between tretinoin and acitretin, *System suitability solution*

Relative standard deviation: NMT 1.0% of acitretin, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{21}H_{26}O_3$ in the portion of Acitretin 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 Acitretin RS in the *Standard solution* (mg/mL)

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

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

IMPURITIES

Inorganic Impurities

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

Organic Impurities

[Note—Store the solutions at 4° before injection.]

- **Procedure**

Mobile phase and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: 0.8 µg/mL each of USP Acitretin RS, USP Acitretin Related Compound A RS, and USP Acitretin Related Compound B RS in alcohol. [Note—Dissolve in tetrahydrofuran before diluting with alcohol.]

Sample solution: 0.25 mg/mL of Acitretin in tetrahydrofuran and alcohol (1:19). [Note—Dissolve in tetrahydrofuran before diluting with alcohol.]

System suitability

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

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 1.5 between acitretin related compound A and acitretin; NLT 1.5 between acitretin related compound B and acitretin

Relative standard deviation: NMT 10.0% for acitretin related compound A and NMT 10.0% for acitretin related compound B

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of acitretin related compound A and acitretin related compound B in the portion of Acitretin taken:

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

r_U = peak response from the relevant impurity from the *Sample solution*

r_S = peak response from the relevant impurity from the *Standard solution*

C_S = concentration of USP Acitretin Related Compound A RS or USP Acitretin Related Compound B RS in the *Standard solution* (µg/mL)

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

Calculate the percentage of impurities other than acitretin related compounds A and B in the portion of Acitretin taken:

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

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

r_S = peak response of USP Acitretin RS in the *Standard solution*

C_S = concentration of USP Acitretin RS in the *Standard solution* (µg/mL)

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

Acceptance criteria

Individual impurities: See *Impurity Table 1*.

Total impurities: NMT 1.0%

Impurity Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Acitretin related compound A	0.78	0.3
Acitretin	1.0	—

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Acitretin related compound B	1.61	0.3
Any unspecified impurity	—	0.1
Total unspecified impurities	—	0.4

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩:** Dry a sample in a vacuum at a pressure not exceeding 19 mm of mercury at 100° for 4 h: it loses NMT 0.2% of its weight.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, protected from light. Store at controlled room temperature.

• **USP Reference Standards ⟨11⟩**

USP Acitretin RS

USP Acitretin Related Compound A RS

(2*Z*,4*E*,6*E*,8*E*)-9-(4-Methoxy-2,3,6-trimethylphenyl)-3,7-dimethylnona-2,4,6,8-tetraenoic acid.

$C_{21}H_{26}O_3$ 326.43

USP Acitretin Related Compound B RS

Ethyl (all-*E*)-9-(4-methoxy-2,3,6-trimethylphenyl)-3,7-dimethylnona-2,4,6,8-tetraenoate.

$C_{23}H_{30}O_3$ 354.48

USP Tretinoin RS

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

Topic/Question	Contact	Expert Committee
ACITRETIN	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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