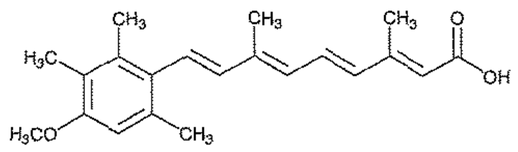
Acitretin



$C_{21}H_{26}O_3$ 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 [55079-83-9].

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

- **A. INFRARED ABSORPTION ⟨197K⟩**
- **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%

Delete the following:

- **HEAVY METALS, *Method II* ⟨231⟩:** NMT 20 ppm (Official 1-Jan-2018)

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%