Impurity Table 1

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

USP Monographs

Acitretin Capsules

DEFINITION

Acitretin Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of acitretin ($C_{21}H_{26}O_3$).

[**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. Make all injections within 1 h of the *Sample solution* preparation.]

IDENTIFICATION

- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

Diluent: Methanol and tetrahydrofuran (13:10)

Mobile phase: Methanol, alcohol, glacial acetic acid, and water (74: 5: 0.5: 21)

Standard solution: 0.1 mg/mL of USP Acitretin RS in a mixture of *Diluent* and water (23:2). Dissolve USP Acitretin RS in *Diluent* equivalent to 80% of the final volume, sonicate for 5 min, add water equivalent to 8% of the final volume, and dilute with *Diluent* to volume.

System suitability solution: Transfer 2 mL of the *Standard solution* to a clear 4-mL glass vial. After sealing the vial with a Teflon-lined silicone septum and cap, place the vial on its side in a light chamber, expose it to 400 foot-candles of fluorescent light for 5 min, and then completely wrap the vial with aluminum foil.

[Note—Exposure to the fluorescent light allows for the formation of two degradation products: acitretin related compound A and 6*Z*-isomer ((2*E*,4*E*,6*Z*,8*E*)-9-(4-methoxy-2,3,6-trimethylphenyl)-3,7-dimethylnona-2,4,6,8-tetraenoic acid).]

Sample solution: Nominally 0.1 mg/mL of acitretin in a mixture of *Diluent* and water (23:2). Open NLT 20 Capsules, composite the Capsule fill, and mix well. Transfer the Capsule fill to a volumetric flask, add water equivalent to 8% of the final volume to wet the sample, and sonicate for 5 min. Dilute with *Diluent* to volume, and sonicate for 5 min. Cool to room temperature, pass the suspension through a suitable filter of 0.5-µm pore size, and use the clear filtrate. [Note—Inject the *Sample solution* within 1 h of preparation.]

Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 365 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.
Column: 4.6-mm × 15-cm; 5-µm packing L1
Flow rate: 1 mL/min
Injection volume: 25 µL

System suitability
Samples: *Standard solution* and *System suitability solution*
[Note—The relative retention times for acitretin related compound A (2*Z*-isomer), acitretin, and the 6*Z*-isomer are 0.84, 1.0, and 1.09, respectively.]
Suitability requirements
Resolution: NLT 3.0 between acitretin related compound A and acitretin; NLT 1.8 between the 6*Z*-isomer and acitretin, *System suitability solution*
Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of acitretin ($C_{21}H_{26}O_3$) in the portion of Capsules taken:

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

r_U = peak response of acitretin from the *Sample solution*
r_S = peak response of acitretin from the *Standard solution*
C_S = concentration of USP Acitretin RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of acitretin in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

- **Dissolution** ⟨711⟩

Test 1
Medium: 3% sodium lauryl sulfate in deaerated water, pH 9.6–10.0; 900 mL
Apparatus 1: 100 rpm
Time: 30 min
Determine the amount of acitretin ($C_{21}H_{26}O_3$) dissolved using the following method.
Standard solution: Transfer about 14 mg of USP Acitretin RS to a 500-mL volumetric flask. Dissolve in 50 mL of alcohol, and dilute with *Medium* to volume.
For Capsules labeled to contain 10 mg: Transfer 20 mL of this solution to a 50-mL volumetric flask, and dilute with *Medium* to volume.
Sample solution: Use portions of the solution under test passed through a suitable filter of 0.45-µm pore size.
Capsule shell solution: Dissolve 6 clean empty-shell Capsules in 900 mL of *Medium*.