Equilibration temperature: 95°
Equilibration time: 15 min
Transfer line temperature: 125°
Pressurization time: 3 min
Carrier gas: Nitrogen
Flow rate: 4.8 mL/min
Injection volume: 1 mL
System suitability
Sample: *Standard solution*
Suitability requirements
Relative standard deviation: NMT 15%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the content, in ppm, of triethylamine in the portion of Adapalene taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 10^6$$

r_U = peak response of triethylamine from the *Sample solution*
r_S = peak response of triethylamine from the *Standard solution*
C_S = concentration of triethylamine in the *Standard solution* (mg/mL)
C_U = concentration of Adapalene in the *Sample solution* (mg/mL)
Acceptance criteria: NMT 80 ppm

SPECIFIC TESTS

- **Loss on Drying** ⟨731⟩
Analysis: Dry a sample at 105° for 4 h.
Acceptance criteria: NMT 0.6%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers, and store at room temperature.
- **Labeling:** If a test for *Organic Impurities* other than *Procedure 1* is used, the labeling states the test with which the article complies.
- **USP Reference Standards** ⟨11⟩
USP Adapalene RS
USP Adapalene Related Compound A RS
Methyl 6-bromo-2-naphthoate.
$C_{12}H_9BrO_2$ 265.10
USP Adapalene Related Compound B RS
Methyl 6-[3-(1-adamantyl)-4-methoxyphenyl]-2-naphthoate.
$C_{29}H_{30}O_3$ 426.55
USP Adapalene Related Compound C RS
2-(Adamant-1-yl)methoxybenzene.
$C_{17}H_{22}O$ 242.36
USP Adapalene Related Compound D RS
4,4′-Dimethoxy-3,3′-di(adamant-1-yl)biphenyl.
$C_{34}H_{42}O_2$ 482.70
USP Adapalene Related Compound E RS
2,2′-Binaphthyl-6,6′-dicarboxylic acid.
$C_{22}H_{14}O_4$ 342.34
USP Triethylamine RS
Triethylamine.
$C_6H_{15}N$ 101.19

Adapalene Gel

DEFINITION

Adapalene Gel contains NLT 90.0% and NMT 110.0% of the labeled amount of adapalene ($C_{28}H_{28}O_3$).

IDENTIFICATION

- **A. Ultraviolet Absorption** ⟨197U⟩
Diluent: Use *Mobile phase* in the *Assay*.
Sample stock solution: Use *Sample stock solution* in the *Assay*.
Sample solution: Nominally equivalent to 0.4 µg/mL of adapalene, prepared as follows. Dilute 2.0 mL of *Sample stock solution* with *Diluent* to 100.0 mL. Pass a portion through a Teflon filter of 0.45-µm pore size and use the filtrate.
Acceptance criteria: Meets the requirements
- **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**
Mobile phase: Acetonitrile, tetrahydrofuran, trifluoroacetic acid, and water (43: 36: 0.02: 21)
Standard stock solution: 0.25 mg/mL of USP Adapalene RS, prepared as follows. Transfer USP Adapalene RS to a suitable volumetric flask, add tetrahydrofuran equivalent to 1% of the final volume, and sonicate to dissolve. Dilute with *Mobile phase* to volume.
Standard solution: 20 µg/mL of USP Adapalene RS in *Mobile phase*, from *Standard stock solution*
Sample stock solution: Nominally equivalent to 20 µg/mL of adapalene, prepared as follows. Transfer 2.0 g of Gel to a 100-mL volumetric flask, add 25 mL of tetrahydrofuran, and sonicate to dissolve. Add 25 mL of acetonitrile and sonicate for 20 min. Cool to room temperature and dilute with *Mobile phase* to volume.
Sample solution: Pass a portion of *Sample stock solution* through a Teflon filter of 0.45-µm pore size and use the filtrate.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 235 nm
Column: 4.6-mm × 25-cm; 5-µm packing L1
Flow rate: 1 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 the labeled amount of adapalene ($C_{28}H_{28}O_3$) in the portion of Gel 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 Adapalene RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of adapalene in the *Sample solution* (mg/mL)
Acceptance criteria: 90.0%–110.0%

IMPURITIES

- **Organic Impurities**
Buffer: 6.8 g/L of monobasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 3.5.
Solution A: *Use Mobile phase* in the *Assay*.
Solution B: *Buffer* and *Solution A* (50:50)
Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	0	100
4	0	100
30	55	45
65	55	45