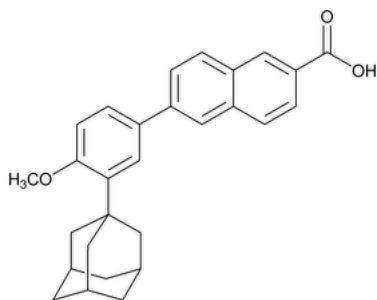


Status: Currently Official on 17-Feb-2025
 Official Date: Official as of 01-May-2020
 Document Type: USP Monographs
 DocId: GUID-7AD2F90B-12C6-45D0-BACD-CDEBB4D16848_4_en-US
 DOI: https://doi.org/10.31003/USPNF_M910_04_01
 DOI Ref: h0i1v

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Adapalene



$C_{28}H_{28}O_3$ 412.52

2-Naphthalenecarboxylic acid, 6-(4-methoxy-3-tricyclo [3.3.1.1^{3,7}]dec-1-ylphenyl)-;

6-[3-(1-Adamantyl)-4-methoxyphenyl]-2-naphthoic acid. CAS RN[®]: 106685-40-9; UNII: 1L4806J2QF.

DEFINITION

Adapalene contains NLT 98.0% and NMT 102.0% of adapalene ($C_{28}H_{28}O_3$), 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

Mobile phase: Acetonitrile, tetrahydrofuran, trifluoroacetic acid, and water (21:16:0.01:13)

Standard stock solution: 0.2 mg/mL of [USP Adapalene RS](#) in *Mobile phase*. Dissolve [USP Adapalene RS](#) in a minimal amount of tetrahydrofuran (about 1%–5% of the final volume), using sonication as needed, and dilute with *Mobile phase* to volume.

Standard solution: 40 µg/mL of [USP Adapalene RS](#) in *Mobile phase* from the *Standard stock solution*

Sample stock solution: 0.2 mg/mL of Adapalene in *Mobile phase*. Dissolve Adapalene in a minimal amount of tetrahydrofuran (about 1%–5% of the final volume), using sonication as needed, and dilute with *Mobile phase* to volume.

Sample solution: 40 µg/mL of Adapalene in *Mobile phase* from the *Sample stock solution*

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

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of adapalene ($C_{28}H_{28}O_3$) in the portion of Adapalene 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* (µg/mL)

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

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

IMPURITIES

- **RESIDUE ON IGNITION (281):** NMT 0.20%

[NOTE—On the basis of the synthetic route, perform either *Organic Impurities, Procedure 1* or *Organic Impurities, Procedure 2*.]

• ORGANIC IMPURITIES, PROCEDURE 1

Procedure 1 is recommended if adapalene related compounds A and B may be present.

Mobile phase: Proceed as directed in the Assay.

Standard stock solution: 0.2 mg/mL of [USP Adapalene RS](#), 0.3 mg/mL of [USP Adapalene Related Compound A RS](#), and 0.2 mg/mL of [USP Adapalene Related Compound B RS](#) in *Mobile phase*. Dissolve [USP Adapalene RS](#), [USP Adapalene Related Compound A RS](#), and [USP Adapalene Related Compound B RS](#) in a minimal amount of tetrahydrofuran (about 1%–5% of the final volume), using sonication as needed, and dilute with *Mobile phase* to volume.

Standard solution: 0.2 µg/mL of [USP Adapalene RS](#), 0.3 µg/mL of [USP Adapalene Related Compound A RS](#), and 0.2 µg/mL of [USP Adapalene Related Compound B RS](#) in *Mobile phase* from the *Standard stock solution*

Sample solution: 0.2 mg/mL of Adapalene in *Mobile phase*. Dissolve Adapalene in a minimal amount of tetrahydrofuran (about 1%–5% of the final volume), using sonication as needed, and dilute with *Mobile phase* to volume.

Chromatographic system: Proceed as directed in the Assay, except use a run time of NLT two times the retention time of adapalene peak for *Standard solution* and NLT six times the retention time of adapalene peak for *Sample solution*.

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 3.0% for the adapalene peak

Column efficiency: NLT 3000 theoretical plates for the adapalene peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of adapalene related compounds A and B in the portion of Adapalene taken:

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

r_U = peak area of each impurity from the *Sample solution*

r_S = peak area of corresponding adapalene related compound A or adapalene related compound B from the *Standard solution*

C_s = concentration of corresponding [USP Adapalene Related Compound A RS](#) or [USP Adapalene Related Compound B RS](#) in the *Standard solution* (mg/mL)

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

Calculate the percentage of each unspecified impurity in the portion of Adapalene taken:

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

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

r_S = peak area of adapalene from the *Standard solution*

C_s = concentration of [USP Adapalene RS](#) in the *Standard solution* (mg/mL)

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

Acceptance criteria: See [Table 1](#). Disregard any impurity peaks less than 0.05%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Adapalene related compound A ^a	0.52	0.10
Adapalene	1.0	