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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

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*: 197U**▲ (CN 1-May-2020)

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
68	0	100
80	0	100

Diluent: Acetonitrile and tetrahydrofuran (3:2)

System suitability stock solution: 0.5 mg/mL of USP Adapalene RS, prepared as follows. Transfer USP Adapalene RS to a suitable volumetric flask, add tetrahydrofuran equivalent to 40% of the final volume, and sonicate to dissolve. Dilute with acetonitrile to volume.

System suitability solution: 0.2 mg/mL of USP Adapalene RS in *Diluent*, from *System suitability stock solution*

Standard solution: 1.0 µg/mL of USP Adapalene RS in *Diluent*, from *System suitability solution*

Sample solution: Nominally equivalent to 0.2 mg/mL of adapalene, prepared as follows. Transfer 5.0 g of Gel to a 25-mL volumetric flask. Add 10 mL of tetrahydrofuran and sonicate to disperse for 10 min. Add 10 mL of acetonitrile and sonicate for 10 min. Cool to room temperature and dilute with acetonitrile to volume. Pass a portion 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

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

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

Suitability requirements

Tailing factor: NMT 2.0, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual impurity in the portion of Gel 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 adapalene 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: See *Table 2*. Disregard any peak less than 0.1%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Adapalene related compound A[a,b]	0.5	—
Adapalene	1.0	—
Adapalene related compound B[b,c]	1.3	—
Any unspecified impurity	—	0.2
Total impurities	—	1.0

[a] Methyl 6-bromo-2-naphthoate.

[b] This process impurity is controlled in the drug substance monograph. It is included in the table for identification only and it is not to be reported in the total impurities.

[c] Methyl 6-[3-(adamant-1-yl)-4-methoxyphenyl]-2-naphthoate.

SPECIFIC TESTS

- **pH** ⟨791⟩**:** 4.0–6.0
- **Minimum Fill** ⟨755⟩**:** Meets the requirements
- **Microbial Enumeration Tests** ⟨61⟩ and **Tests for Specified Microorganisms** ⟨62⟩**:** The total aerobic microbial count is NMT 10^2 cfu/g. The total yeasts and molds count is NMT 10^1 cfu/g. It meets the requirements of the tests for the absence of *Escherichia coli*, *Salmonella* species, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* species.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers. Store at controlled room temperature and protect from freezing.
- **USP Reference Standards** ⟨11⟩
  USP Adapalene RS

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

Topic/Question	Contact	Expert Committee
ADAPALENE GEL	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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