



Adapalene and Benzoyl Peroxide Gel

Type of Posting	Revision Bulletin
Posting Date	27-Mar-2026
Official Date	1-Apr-2026
Expert Committee	Small Molecules 1

In accordance with the Rules and Procedures of the Council of Experts, the Small Molecules 1 Expert Committee has revised the Adapalene and Benzoyl Peroxide Gel monograph. The purpose of this revision is to widen the *pH* requirement from 3.0–4.7 to 3.0–6.0 to accommodate FDA-approved products with wider specifications.

The Adapalene and Benzoyl Peroxide Gel Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Tsion Billign, Principal Scientist (301-816-8286 or tb@usp.org).

Adapalene and Benzoyl Peroxide Gel

DEFINITION

Adapalene and Benzoyl Peroxide Gel contains NLT 90.0% and NMT 110.0% of the labeled amount of adapalene ($C_{28}H_{28}O_3$) and NLT 90.0% and NMT 115.0% of the labeled amount of benzoyl peroxide ($C_{14}H_{10}O_4$).

IDENTIFICATION

- **A.** The retention times of adapalene and benzoyl peroxide of the respective *Sample solution* correspond to those of the respective *Standard solution*, as obtained in the *Assay, Adapalene* and the *Assay, Benzoyl Peroxide*.
- **B.** The UV spectra of adapalene and benzoyl peroxide of the respective *Sample solution* correspond to those of the respective *Standard solution*, as obtained in the *Assay, Adapalene* and the *Assay, Benzoyl Peroxide*.

ASSAY

• ADAPALENE

Protect solutions containing adapalene from light.

Mobile phase: [Acetonitrile](#), [tetrahydrofuran](#), [glacial acetic acid](#), and [water](#) (40: 30: 0.5: 30)

Diluent: [Acetonitrile](#), [tetrahydrofuran](#), [glacial acetic acid](#), and [water](#) (40: 25: 0.5: 30)

Standard stock solution: 0.4 mg/mL of [USP Adapalene RS](#) in [tetrahydrofuran](#)

Standard solution: 0.02 mg/mL of [USP Adapalene RS](#) from *Standard stock solution* in *Diluent*

Sample solution: Nominally 0.02 mg/mL of adapalene in *Diluent*, prepared as follows. Transfer a suitable quantity of Gel, nominally equivalent to NLT 1 mg of adapalene, to a suitable volumetric flask, add 5% of the flask volume of [tetrahydrofuran](#), and vortex until all lumps are completely dissolved. Add 10% of the flask volume of *Diluent* and vortex. Let the sample solution stand for 10 min and immediately after, dilute with *Diluent* to volume. Pass through a suitable filter of 0.45- μ m pore size.

Chromatographic system

(See [Chromatography](#) (621), [System Suitability](#).)

Mode: LC

Detector: UV 270 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm \times 5-cm; 3.5- μ m packing [L1](#)

Column temperature: 23°

Flow rate: 1 mL/min

Injection volume: 10 μ L

Run time: NLT 1.5 times the retention time of adapalene

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

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 of adapalene from the *Sample solution*

r_S = peak response 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: 90.0%–110.0%

• BENZOYL PEROXIDE

[**CAUTION**—Benzoyl Peroxide is a strong oxidizer. It reacts violently with organic and inorganic acids, alcohols and amines, and combustible materials.]

Mobile phase: [Acetonitrile](#) and [water](#) (60:40)

Standard stock solution: Weigh and transfer 335 mg of [benzoyl peroxide, 75 percent](#) to a 100-mL volumetric flask, dissolve, and dilute with [acetonitrile](#) to volume. The concentration of benzoyl peroxide is determined using potentiometric titration as follows.

Titrimetric system

(See [Titrimetry](#) (541).)

Potassium iodide solution: 166 mg/mL of [potassium iodide](#) in [water](#)

Blank: To a suitable titration vessel, add 45 mL of [acetonitrile](#) and 1 mL of *Potassium iodide solution*. Cover and mix the solution for NLT 15 min. Protect against actinic light.

Mode: Direct titration

Titrant: 0.01 N sodium thiosulfate VS. Prepare daily from [0.1 N sodium thiosulfate VS.](#)

End point detection: Potentiometric

Analysis: Transfer 5 mL of the *Standard stock solution* to a suitable titration vessel, add 40 mL of [acetonitrile](#), and 1 mL of *Potassium iodide solution*. Cover and mix the solution for NLT 15 min. Protect against actinic light. [NOTE—It is suggested to titrate using a suitable combined platinum ring redox electrode or using a platinum ring electrode in combination with a suitable reference electrode.]

Calculate the concentration (mg/mL) of benzoyl peroxide ($C_{14}H_{10}O_4$) in the *Standard stock solution*:

$$\text{Result} = [(V_S - V_B) \times (N/2) \times F]/V_{STD}$$

V_S = volume of *Titrant* consumed by the *Standard stock solution* (mL)

V_B = volume of *Titrant* consumed by the *Blank* (mL)

N = actual concentration of *Titrant*, in normality (mEq/mL)

F = equivalency factor of benzoyl peroxide, 242.23 (mg/mEq)

V_{STD} = volume of *Standard stock solution* taken, 5 mL

Standard solution: 0.125 mg/mL of benzoyl peroxide from the *Standard stock solution* in [acetonitrile](#)

Sample solution: Nominally 0.125 mg/mL of benzoyl peroxide in [acetonitrile](#), prepared as follows.

Transfer a suitable quantity of Gel, equivalent to NLT 12.5 mg of benzoyl peroxide, to a suitable volumetric flask, add 25% of the flask volume of [acetonitrile](#), and shake for NLT 15 min. Dilute with [acetonitrile](#) to volume. Pass through a suitable filter of 0.45- μ m pore size.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 235 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Columns

Guard: 3.9-mm × 2-cm; 5-μm packing [L1](#)

Analytical: 4.6-mm × 25-cm; 5-μm packing [L1](#)

Column temperature: 23°

Flow rate: 1 mL/min

Injection volume: 10 μL

Run time: NLT 2 times the retention time of benzoyl peroxide

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of benzoyl peroxide ($C_{14}H_{10}O_4$) in the portion of Gel taken:

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

r_U = peak response of benzoyl peroxide from the *Sample solution*

r_S = peak response of benzoyl peroxide from the *Standard solution*

C_S = concentration of benzoyl peroxide in the *Standard solution* (mg/mL)

C_U = nominal concentration of benzoyl peroxide in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–115.0%

IMPURITIES

• ORGANIC IMPURITIES, ADAPALENE

Protect the solutions containing adapalene from light.

Solution A: [Acetonitrile](#), [tetrahydrofuran](#), [trifluoroacetic acid](#), and [water](#) (40: 5: 0.2: 55)

Solution B: [Acetonitrile](#), [tetrahydrofuran](#), [trifluoroacetic acid](#), and [water](#) (55: 35: 0.2: 10)

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
4	56	44
6	56	44

Time (min)	Solution A (%)	Solution B (%)
9	0	100
10	0	100
10.1	100	0
13	100	0

Diluent: [Acetonitrile](#), [tetrahydrofuran](#), and [water](#) (36:24:40)

Buffer A: [Trifluoroacetic acid](#) and [water](#) (0.2: 100)

Buffer B: 49.6 g/L of [sodium thiosulfate](#) (pentahydrate) in [water](#)

Standard stock solution 1: 0.5 mg/mL of [USP Adapalene RS](#) in [tetrahydrofuran](#)

Standard stock solution 2: 0.01 mg/mL of [USP Adapalene RS](#) from *Standard stock solution 1* in *Diluent*

Impurity stock solution: 0.2 mg/mL of [USP Adapalene Related Compound C RS](#), prepared as follows.

Weigh and transfer a suitable quantity of [USP Adapalene Related Compound C RS](#) to a suitable volumetric flask, add 50% of the flask volume of [tetrahydrofuran](#), and sonicate for NLT 10 min. Add 10% of the flask volume of [water](#), and sonicate for NLT 5 min. Dilute with [tetrahydrofuran](#) to volume.

Impurity solution: 0.02 mg/mL of [USP Adapalene Related Compound C RS](#) from *Impurity stock solution* in *Diluent*

System suitability solution: 1.25 mg/mL of benzoyl peroxide, 0.5 µg/mL of [USP Adapalene Related Compound C RS](#), and 0.05 mg/mL of [USP Adapalene RS](#), prepared as follows. Weigh and transfer a suitable quantity of [benzoyl peroxide, 75 percent](#) to a suitable volumetric flask, add 2.5% of the flask volume of *Impurity solution*, 10% of the flask volume of *Standard stock solution 1*, and add 12.5% of the flask volume of [methanol](#). Mix between additions. Add 25% of the flask volume of *Buffer B* and mix. Wait for 60 min. Then add 35% of the flask volume of [acetonitrile](#) and mix. Dilute with *Buffer A* to volume. Pass through a suitable filter of 0.2-µm pore size.

Standard solution: 0.001 mg/mL of [USP Adapalene RS](#) from *Standard stock solution 2*, prepared as follows. Dilute a suitable volume of *Standard stock solution 2* in a suitable volumetric flask. Add 12.5% of the flask volume of [tetrahydrofuran](#), 12.5% of the flask volume of [methanol](#), 25% of the flask volume of *Buffer B*, and 35% of the flask volume of [acetonitrile](#). Dilute with [water](#) to volume.

Sensitivity solution: 0.025 µg/mL of [USP Adapalene RS](#) from *Standard stock solution 2*, prepared as mentioned in the *Standard solution*

Sample solution: Nominally 0.05 mg/mL of adapalene, prepared as follows. Transfer a suitable quantity of Gel, nominally equivalent to NLT 1 mg of adapalene, to a suitable volumetric flask. Add 12.5% of the flask volume of [tetrahydrofuran](#) and mix for NLT 5 min with vortex. Add 12.5% of the flask volume of [methanol](#) and mix for NLT 5 min with vortex. Add 25% of the flask volume of *Buffer B* and mix for 5 min with vortex. Wait for 60 min. Then add 35% of the flask volume of [acetonitrile](#) and mix. Dilute with *Buffer A* to volume. Pass through a suitable filter of 0.2-µm pore size.

Chromatographic system

(See [Chromatography](#) (621), [System Suitability](#).)

Mode: LC

Detector: UV 270 nm

Column: 3.0-mm × 5-cm; 1.8-μm packing [L1](#)

Column temperature: 50°

Flow rate: 0.8 mL/min

Injection volume: 20 μL

System suitability

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

[NOTE—The relative retention times in [Table 2](#) are provided as information that could aid in peak assignment.]

Table 2

Name	Relative Retention Time
Binaphthyl acid ^a	0.17
Hydroxyadapalene ^b	0.39
Adapalene related compound C	0.94
Adapalene	1.0
Bisadamantyl anisole ^c	1.56

^a 2,2'-Binaphthyl-6,6'-dicarboxylic acid.

^b 6-[3-(3-Hydroxyadamantan-1-yl)-4-methoxyphenyl]-2-naphthoic acid.

^c 4,4'-Dimethoxy-3,3'-di(adamantan-1-yl)biphenyl.

Suitability requirements

Resolution: NLT 2.3 between adapalene related compound C and adapalene, *System suitability solution*

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

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution and Sample solution*

Calculate the percentage of any unspecified degradation product in the portion of Gel taken:

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

r_U = peak response of each unspecified degradation product from the *Sample solution*

r_S = peak response 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: The reporting threshold is 0.05%.

Any unspecified degradation product: NMT 0.21%

Total degradation products: NMT 1%

• ORGANIC IMPURITIES, BENZOYL PEROXIDE

Solution A: [Glacial acetic acid](#) and [water](#) (1:1000)

Solution B: [Glacial acetic acid](#) and [acetonitrile](#) (1:1000)

Mobile phase: See [Table 3](#).

Table 3

Time (min)	Solution A (%)	Solution B (%)
0	82	18
10	40	60
22	40	60
22.1	0	100
28	0	100
28.1	82	18
33	82	18

Sensitivity solution: 1 µg/mL of [USP Benzoic Acid RS](#) in [acetonitrile](#)

Standard solution: 0.1 mg/mL of [USP Benzoic Acid RS](#) and 0.02 mg/mL each of [USP Ethyl Benzoate RS](#) and [USP Benzaldehyde RS](#) in [acetonitrile](#)

Sample solution 1: Nominally 2 mg/mL of benzoyl peroxide, prepared as follows. Transfer a suitable quantity of Gel, nominally equivalent to NLT 50 mg of benzoyl peroxide, to a suitable volumetric flask. Add 40% of the flask volume of [acetonitrile](#) and mix for 5 min or to complete dissolution of the product on a vortex-type mixer. Dilute with [acetonitrile](#) to volume. Pass through a suitable filter of 0.45-µm pore size.

[NOTE—This solution is used for the quantification of ethyl benzoate, benzaldehyde, and any unspecified degradation product.]

Sample solution 2: Nominally 0.4 mg/mL of benzoyl peroxide from *Sample solution 1* in [acetonitrile](#)

[NOTE—This solution is used for the quantification of benzoic acid.]

Chromatographic system

(See [Chromatography](#) (621), [System Suitability](#).)

Mode: LC

Detector: UV 235 nm

Column: 3.9-mm × 15-cm; 5-µm packing [L1](#)

Column temperature: 22°

Flow rate: 1.2 mL/min

Injection volume: 10 µL

System suitability

Samples: *Sensitivity solution* and *Standard solution*

[NOTE—The relative retention times in [Table 4](#) are provided as information that could aid in peak assignment.]

Table 4

Name	Relative Retention Time
Benzoic acid	0.37
Benzaldehyde	0.45
Ethyl benzoate	0.73
Benzoyl peroxide	1.0

Suitability requirements

Resolution: NLT 3 between benzoic acid and benzaldehyde, *Standard solution*

Relative standard deviation: NMT 2% for benzoic acid; NMT 5% each for benzaldehyde and ethyl benzoate, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution, Sample solution 1, and Sample solution 2*

Calculate the percentage of benzoic acid in the portion of Gel taken:

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

r_U = peak response of benzoic acid from *Sample solution 2*

r_S = peak response of benzoic acid from the *Standard solution*

C_S = concentration of [USP Benzoic Acid RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of benzoyl peroxide in *Sample solution 2* (mg/mL)

Calculate the percentage of benzaldehyde in the portion of Gel taken:

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

r_U = peak response of benzaldehyde from *Sample solution 1*

r_S = peak response of benzaldehyde from the *Standard solution*

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

C_U = nominal concentration of benzoyl peroxide in *Sample solution 1* (mg/mL)

Calculate the percentage of ethyl benzoate in the portion of Gel taken:

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

r_U = peak response of ethyl benzoate from *Sample solution 1*

r_S = peak response of ethyl benzoate from the *Standard solution*

C_S = concentration of [USP Ethyl Benzoate RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of benzoyl peroxide in *Sample solution 1* (mg/mL)

Calculate the percentage of any unspecified degradation product in the portion of Gel taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each unspecified degradation product from *Sample solution 1*

- r_S = peak response of benzoic acid from the *Standard solution*
 C_S = concentration of [USP Benzoic Acid RS](#) in the *Standard solution* (mg/mL)
 C_U = nominal concentration of benzoyl peroxide in *Sample solution 1* (mg/mL)
 F = relative response factor of benzoic acid against benzoyl peroxide, 1.56

Acceptance criteria: See [Table 5](#). The reporting threshold is 0.05%. [NOTE—The peaks beyond a relative retention time of 1.47 were not considered.]

Table 5

Name	Acceptance Criteria, NMT (%)
Benzoic acid	17.0
Benzaldehyde	0.25
Ethyl benzoate	0.25
Any unspecified degradation product	0.20
Total degradation products	17.0

SPECIFIC TESTS

Change to read:

- [pH](#) (791): ▲3.0–6.0▲ (RB 1-Apr-2026)
- [MICROBIAL ENUMERATION TESTS](#) (61) and [TESTS FOR SPECIFIED MICROORGANISMS](#) (62): The total aerobic microbial count is NMT 10² cfu/g. The total combined yeasts and molds count is NMT 10¹ cfu/g. It meets the requirements of the tests for absence of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and bile-tolerant Gram-negative bacteria.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers. Store at controlled room temperature. Keep away from heat.

- [USP REFERENCE STANDARDS](#) (11).

[USP Adapalene RS](#)

[USP Adapalene Related Compound C RS](#)

2-(Adamantan-1-yl)methoxybenzene.

$C_{17}H_{22}O$ 242.36

[USP Benzaldehyde RS](#)

[USP Benzoic Acid RS](#)

[USP Ethyl Benzoate RS](#)

Ethyl Benzoate.

$C_9H_{10}O_2$ 150.18

Page Information:

Not Applicable

Current DocID:

© 2026 The United States Pharmacopeial Convention *All Rights Reserved.*