Microbial enumeration tests ⟨61⟩ **and Tests for specified microorganisms** ⟨62⟩**—**It meets the requirements of the tests for absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa.*

Minimum fill ⟨755⟩: meets the requirements.

Assay—

Mobile phase—Mix approximately equal volumes of acetonitrile and water, adjusting the ratio of solvents as necessar y to achieve acceptable chromatography.

Internal standard solution—Dissolve Butylparaben in acetonitrile to obtain a solution having a concentration of 6 µg per mL.

Standard preparation—Dissolve an accurately weighed quantity of USP Halcinonide RS in *Internal standard solution* to obtain a solution having a known concentration of about 0.04 mg per mL. Mix 5.0 mL of this solution with 5.0 mL of the *Mobile phase*. Each mL of the *Standard preparation* has a known concentration of about 0.02 mg of USP Halcinonide RS .

Assay preparation—Transfer an accurately weighed quantity of Ointment, equivalent to about 1 mg of halcinonide, to a glass-stoppered, 50-mL centrifuge tube, and add 25.0 mL of *Internal standard solution* and 5.0 mL of hexane. Place in a water bath at 58 ± 2° for 3 minutes, then mix in a vortex mixer for about 1 minute until the specimen is well dispersed. Repeat the above-specified heating and mixing step one more time. Cool in an ice-methanol bath for 15 minutes or until the two phases separate, centrifuging if necessar y. Transfer 5.0 mL of the lower layer into a 15-mL centrifuge tube, add 5.0 mL of *Mobile phase*, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 3.9-mm × 30-cm column that contains packing L1. The flow rate is about 2 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed under *Procedure:* the resolution, *R,* between the analyte and internal standard peaks is not less than 2.0, and the relative standard deviation for replicate injections is not more than 3.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. The relative retention times are about 0.6 for butylparaben and 1.0 for halcinonide. Calculate the quantity, in mg, of $C_{24}H_{32}ClFO_5$ in the portion of Ointment taken by the formula:

$$50C(R_U / R_S)$$

in which *C* is the concentration, in mg per mL, of USP Halcinonide RS in the *Standard preparation;* and R_U and R_S are the ratios of the peak responses of halcinonide to internal standard obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Halcinonide Topical Solution

» Halcinonide Topical Solution is Halcinonide in a suitable aqueous vehicle. It contains not less than 90.0 percent and not more than 110.0 per cent of the labeled amount of $C_{24}H_{32}ClFO_5$.

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩**—**
USP Halcinonide RS

Identification—It responds to the *Identification* test under *Halcinonide Cream*.

Microbial enumeration tests ⟨61⟩ **and Tests for specified microorganisms** ⟨62⟩**—**It meets the requirements of the tests for absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa.*

Assay—

Mobile phase—Mix approximately equal volumes of acetonitrile and water, adjusting the ratio of solvents as necessar y to achieve acceptable chromatography.

Internal standard solution—Transfer 15 mg of Progesterone to a 50-mL volumetric flask. Dissolve in *Mobile phase*, dilute with *Mobile phase* to volume, and mix.

Standard preparation—Transfer about 20 mg of USP Halcinonide RS, accurately weighed, to a 100-mL volumetric flask, dissolve in *Mobile phase*, dilute with *Mobile phase* to volume, and mix. Transfer 5.0 mL of this solution to a 50-mL volumetric flask, add 2.0 mL of *Internal standard solution*, dilute with *Mobile phase* to volume, and mix.

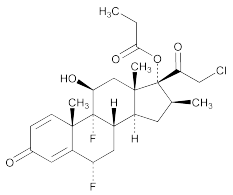
Assay preparation—Transfer an accurately measured quantity of Topical Solution, equivalent to about 1 mg of halcinonide, to a 50-mL volumetric flask, add 2.0 mL of *Internal standard solution*, dilute with *Mobile phase* to volume, and mix.

Chromatographic system and *Procedure*—Proceed as directed in the *Assay* under *Halcinonide Cream*. Calculate the quantity, in mg, of $C_{24}H_{32}ClFO_5$ in the portion of T opical Solution taken by the formula:

$$50C(R_U / R_S)$$

in which the terms are as defined therein.

Halobetasol Propionate



$C_{25}H_{31}ClF_2O_5$ 484.96

Pregna-1,4-diene-3,20-dione, 21-chloro-6,9-difluoro-11-hydroxy-16-methyl-17-(1-oxopropoxy)-, (6α,11β,16β)-;
21-Chloro-6α,9-difluoro-11β,17-dihydroxy-16β-methylpregna-1,4-diene-3,20-dione 17-propionate [66852-54-8].

DEFINITION

Halobetasol Propionate contains NLT 98.0% and NMT 102.0% of $C_{25}H_{31}ClF_2O_5$, calculated on the dried basis.

IDENTIFICATION

- **A. Infrared Absorption** ⟨197K⟩
- **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**

Solution A: Acetonitrile and water (9:11)
Solution B: Acetonitrile
Mobile phase: See the gradient table below.

Time (min)	Solution A (%)	Solution B (%)
0	100	0
2	64.5	35.5
22	64.5	35.5
23	100	0
30	100	0

Standard solution: 0.2 mg/mL of USP Halobetasol Propionate RS in acetonitrile
Sample solution: 0.2 mg/mL of Halobetasol Propionate in acetonitrile
Chromatographic system
(See *Chromatography* ⟨621⟩*, System Suitability*.)
Mode: LC
Detector: UV 240 nm
Column: 4.6-mm × 25-cm; 5-µm packing L1
Column temperature 40°
Flow rate: 0.8 mL/min
Injection size: 20 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Relative standard deviation: NMT 2.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of $C_{25}H_{31}ClF_2O_5$ in the portion of Halobetasol Propionate 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 the *Standard solution* (mg/mL)
C_U = concentration of the *Sample solution* (mg/mL)
Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

Inorganic Impurities
- **RESIDUE ON IGNITION** ⟨**281**⟩**:** NMT 0.2%
- **HEAVY METALS,** *Method II* ⟨**231**⟩**:** NMT 20 ppm

Organic Impurities
- **PROCEDURE**

Mobile phase, Standard solution, and **Sample solution:** Proceed as directed in the *Assay*.
Chromatographic system
(See *Chromatography* ⟨621⟩*, System Suitability*.)
Mode: LC
Detector: UV 240 nm
Column: 4.6-mm × 25-cm; 5-µm packing L1
Column temperature: 40°
Flow rate: 0.8 mL/min
Injection size: 20 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Column efficiency: NLT 22,000 theoretical plates
Tailing factor: NLT 0.9 and NMT 1.1 for halobetasol propionate
Relative standard deviation: NMT 2.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of any impurity in the portion of Halobetasol Propionate taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response of any individual impurity from the *Sample solution*
r_T = sum of responses for all the peaks from the *Sample solution*

Acceptance criteria
Individual impurities: See *Impurity Table 1*.
Total impurities: NMT 1.0%

Impurity Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
21-Chloro diflorasone[a]	0.75	0.15
21-Acetate 17-propionate diflorasone[b]	0.88	0.15
11-Propionate 21- chloro diflorasone[c]	0.95	0.15
Halobetasol propionate	1.0	—
9-Chloro halobetasol propionate[d]	1.12	0.15
6-Chloro halobetasol propionate[e]	1.24	0.15
Any individual, unspecified degradation product	—	0.10

[a] 21-Chloro-6α,9-difluoro-11β,17-dihydroxy-16β-methylpregna-1,4-diene-3,20-dione.
[b] 6α,9-Difluoro-11β,17,21-trihydroxy-16β-methylpregna-1,4-diene-3,20-dione 21-acetate 17-propionate.
[c] 21-Chloro-6α,9-difluoro-11β,17-dihydroxy-16β-methylpregna-1,4-diene-3,20-dione 11-propionate.
[d] 9,21-Dichloro-6α,-fluoro-11β,17-dihydroxy-16β-methylpregna-1,4-diene-3,20-dione 17-propionate.
[e] 6α,21-Dichloro-9-fluoro-11β,17-dihydroxy-16β-methylpregna-1,4-diene-3,20-dione 17-propionate.

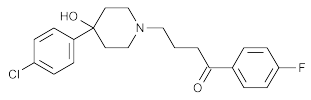
SPECIFIC TESTS

- **LOSS ON DRYING** ⟨**731**⟩**:** Dry a sample in a vacuum at 70 ° for 3 h: it loses NMT 1.0% of its weight.
- **OPTICAL ROTATION,** *Specific Rotation* ⟨**781S**⟩
Sample solution: 10 mg/mL in dioxane
Acceptance criteria Between +87° and +99°

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed, light resistant containers. Store between 2 ° and 8 °.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Halobetasol Propionate RS
Pregna-1,4-diene-3,20-dione, 21-chloro-6,9-difluoro-11-hydroxy-16-methyl-17-(1-oxopropoxy)-, (6α,11β,16β)-.
21-Chloro-6α,9-difluoro-11β,17-dihydroxy-16β-methylpregna-1,4-diene-3,20-dione 17-propionate.
$C_{25}H_{31}ClF_2O_5$ 484.96

Haloperidol



$C_{21}H_{23}ClFNO_2$ 375.86
1-Butanone, 4-[4-(4-chlorophenyl)-4-hydroxy-1-piperidinyl]-1-(4-fluorophenyl)-.
4-[4-(*p*-Chlorophenyl)-4-hydroxypiperidino]-4′-fluorobutyrophenone [52-86-8].

» Haloperidol contains not less than 98.0 per cent and not more than 102.0 per cent of $C_{21}H_{23}ClFNO_2$, calculated on the dried basis.

Packaging and storage—Preserve in tight, light-resistant containers.