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Halcinonide Cream

DEFINITION

Halcinonide Cream is Halcinonide in a suitable cream base. It contains NLT 90.0% and NMT 110.0% of the labeled amount of halcinonide ($C_{24}H_{32}ClFO_5$).

IDENTIFICATION

• **A.** The retention time of the halcinonide peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

• **B.** The UV-Vis spectrum of the halcinonide peak of the *Sample solution* corresponds to that of the *Diluted standard stock solution*, as obtained in the test for *Organic Impurities*.

ASSAY

• **Procedure**

Mobile phase: Acetonitrile and water (50:50)

Diluent: Acetonitrile and water (2:1), saturated with hexanes. [Note—Prepare on the day of use.]

Internal standard solution: 150 µg/mL of progesterone in hexanes-saturated *Diluent*

Standard stock solution: 0.2 mg/mL of USP Halcinonide RS in *Diluent*

Standard solution: 0.02 mg/mL of USP Halcinonide RS in hexanes-saturated *Diluent* prepared as follows. Transfer 5.0 mL of *Standard stock solution* to a 50-mL volumetric flask. Add 4.0 mL of *Internal standard solution*, and dilute with hexanes-saturated *Diluent* to volume.

Sample solution: Nominally 0.02 mg/mL of halcinonide in hexanes-saturated *Diluent* prepared as follows. Transfer a quantity of Cream equivalent to 0.5 mg of halcinonide to a glass-stoppered, 50-mL centrifuge tube. Add 12 mL of hexanes-saturated *Diluent* and 20 mL of hexanes, and shake for 1 min. Place in a heated ultrasonic bath at 58 ± 2° for 20 min, initially shaking for 1–2 min to ensure dispersion, and at 5-min intervals thereafter, on a vibratory mixer. Cool, centrifuge, and transfer the lower layer to a 25-mL volumetric flask. Add 5 mL of hexanes-saturated *Diluent* to the tube, mix for 1 min, then centrifuge. Transfer the lower layer to the volumetric flask, and repeat the extraction with an additional 5 mL of hexanes-saturated *Diluent*, combining the extracts in the flask. Add 2.0 mL of *Internal standard solution* to the flask, dilute with hexanes-saturated *Diluent* to volume, and mix. If necessary, clarify a portion of the solution by centrifugation.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 254 nm

Column: 4-mm × 30-cm; packing L1

Flow rate: 2 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

[Note—The relative retention times for halcinonide and progesterone are 1.0 and 1.2, respectively.]

Suitability requirements

Resolution: NLT 1.5 between halcinonide and progesterone

Relative standard deviation: NMT 3.0%, peak response ratio of halcinonide to progesterone

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of halcinonide ($C_{24}H_{32}ClFO_5$) in the portion of Cream taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = peak response ratio of halcinonide to progesterone from the *Sample solution*

R_S = peak response ratio of halcinonide to progesterone from the *Standard solution*

C_S = concentration of USP Halcinonide RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Minimum Fill ⟨755⟩:** Meets the requirements

IMPURITIES

• **Organic Impurities**

Solution A: 10 mM of ammonium acetate in water

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
20.0	10	90
22.0	10	90
22.1	90	10
25.0	90	10

Diluent 1: Acetonitrile and water (60:30), saturated with hexanes

Diluent 2: Acetonitrile and water (10:90)

Standard stock solution: 0.2 mg/mL of USP Halcinonide RS in *Diluent 1*

Diluted standard stock solution: 0.1 mg/mL of USP Halcinonide RS in *Diluent 2* from the *Standard stock solution*

Standard solution: 0.2 µg/mL of USP Halcinonide RS in *Diluent 2* from the *Standard stock solution*

Sample stock solution: Nominally 0.2 mg/mL of halcinonide in *Diluent 1* prepared as follows. Transfer a portion of Cream equivalent to 4 mg of halcinonide to a 50-mL centrifuge tube. Add 10 mL of *Diluent 1* and 20 mL of hexanes heated at 58 ± 2° for 20 min. Shake for NLT 1 min initially to ensure dispersion and at 5-min intervals thereafter. Cool, centrifuge at 3000 rpm for 10 min, and transfer the lower layer to the 20-mL volumetric flask. Repeat the extraction with an additional 5 mL of *Diluent 1* and 20 mL of hexanes each time. Dilute with *Diluent 1* to volume.

Sample solution: 0.1 mg/mL of halcinonide from *Sample stock solution* in *Diluent 2*

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 240 nm. For *Identification* test *B*, use a diode array detector in the range of 200–450 nm.

Column: 2.1-mm × 15-cm; 1.7-µm packing L1

Flow rate: 0.3 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

[Note—See *Table 2* for relative retention times.]

Suitability requirements

Relative standard deviation: NMT 2.4%

Signal-to-noise ratio: NLT 50

Analysis

Samples: *Diluted standard stock solution*, *Standard solution*, and *Sample solution*

[Note—The *Diluted standard stock solution* is used for *Identification* test *B*.]

Calculate the percentage of any individual unspecified impurity in the portion of Cream taken:

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

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

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

C_S = concentration of USP Halcinonide RS in the *Standard solution* (µg/mL)

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

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Dihydrotriamcinolone[a]	0.5	—
Halcinonide	1.0	—
Any individual unspecified impurity	—	0.2
Total impurities	—	3.0

[a] Drug substance process impurity included in the table for identification only.

SPECIFIC TESTS

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** Meets the requirements for absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa*

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store at room temperature. Avoid excessive heat.

• **USP Reference Standards ⟨11⟩**

USP Halcinonide RS

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

Topic/Question	Contact	Expert Committee
HALCINONIDE CREAM	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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