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Hydrocortisone Gel

DEFINITION

Hydrocortisone Gel is Hydrocortisone in a suitable hydroalcoholic gel base. It contains NLT 90.0% and NMT 110.0% of the labeled amount of hydrocortisone ($C_{21}H_{30}O_5$).

IDENTIFICATION

Delete the following:

▲• *Thin-Layer Chromatographic Identification Test* ⟨201⟩

Sample solution: Transfer a quantity of Gel, equivalent to 5 mg of hydrocortisone, to a flask. Add 5 mL of alcohol, and heat on a steam bath for 5 min, with frequent shaking. Cool, and filter. Use the filtrate.

Acceptance criteria: Meets the requirements▲ (USP 1-May-2020)

Add the following:

▲• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2020)

Add the following:

▲• **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2020)

ASSAY

Change to read:

• ▲Procedure

Solution A: 0.1% glacial acetic acid in water

Solution B: 0.1% glacial acetic acid in acetonitrile

Solution C: Acetonitrile, glacial acetic acid, and water (40:1:60)

Solution D: Tetrahydrofuran and water (50:50)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0.0	74	26
11.0	74	26
20.0	55	45
30.0	30	70
30.1	74	26
35.0	74	26

Diluent: *Solution C* and *Solution D* (80:20)

System suitability solution: 0.3 mg/mL of USP Hydrocortisone RS and 6 µg/mL of USP Prednisolone RS in *Diluent*. Sonicate to dissolve, if necessary.

Standard solution: 0.3 mg/mL of USP Hydrocortisone RS in *Diluent*. Sonicate to dissolve, if necessary.

Sample solution: Nominally 0.3 mg/mL of hydrocortisone prepared as follows. Transfer 3 mg of hydrocortisone from a portion of Gel to a 10-mL volumetric flask. Add 2 mL of *Solution D* and vortex for about 3 min or until the sample is thoroughly dispersed. Add about 6 mL of *Solution C* and sonicate for about 10 min with intermittent vortexing and shaking. Dilute with *Solution C* to volume. Centrifuge a portion of the solution to obtain a clear supernatant. [NOTE—The use of a centrifuge speed of 3500 rpm for 30 min may be suitable.] Use the supernatant.

Chromatographic system

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

Mode: LC

Detector: UV 246 nm. For *Identification B*, use a diode array detector in the range of 210–400 nm.

Column: 4.6-mm × 15-cm; 3-µm packing L1

Column temperature: 30°

Flow rate: 0.8 mL/min

Injection volume: 10 µL

System suitability

Samples: *System suitability solution* and *Standard solution* [NOTE—See *Table 2* for relative retention times.]

Suitability requirements

Resolution: NLT 1.5 between hydrocortisone and prednisolone, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of hydrocortisone ($C_{21}H_{30}O_5$) 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 Hydrocortisone RS in the *Standard solution* (mg/mL)

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

▲ (USP 1-May-2020)

Acceptance criteria: 90.0%–110.0%

IMPURITIES

Add the following:

▲• **ORGANIC IMPURITIES**

Solution A, Solution B, Solution C, Solution D, Mobile phase, Diluent, System suitability solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Sensitivity solution: 0.3 µg/mL of USP Hydrocortisone RS in *Diluent*. Sonicate to dissolve, if necessary.

Standard solution: 0.0015 mg/mL of USP Hydrocortisone RS in *Diluent*. Sonicate to dissolve, if necessary.

System suitability

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

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

Suitability requirements

Resolution: NLT 1.5 between hydrocortisone and prednisolone, *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 cortisone or hydrocortisone glyoxal analog 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 cortisone or hydrocortisone glyoxal analog from the *Sample solution*

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

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

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

F = relative response factor (see *Table 2*)

Calculate the percentage of each unspecified impurity 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 impurity from the *Sample solution*

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

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

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

Acceptance criteria: See *Table 2*. The reporting threshold is 0.1%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
6β-Hydroxyhydrocortisone[a,b]	0.27	—	—
7α-Hydroxyhydrocortisone[c,b]	0.33	—	—
Hydrocortisone glyoxal analog[d]	0.81	0.89	0.5
Hydrocortisone-6-ene[e,b]	0.87	—	—
Prednisolone[b]	0.95	—	—
Hydrocortisone	1.00	—	—
Cortisone[f]	1.16	0.96	0.5
Cortodoxone[g,b]	1.79	—	—
Hydrocortisone acetate[b]	1.92	—	—
Any individual unspecified impurity	—	—	0.5
Total impurities	—	—	2.0

[a] 6β,11β,17,21-Tetrahydroxypregn-4-ene-3,20 dione.

[b] Process impurity included in the table for identification only. Process impurities are controlled in the drug substance and are not to be reported or included in the total impurities of the drug product.

[c] 7α,11β,17,21-Tetrahydroxypregn-4-ene-3,20-dione.

[d] 11β,17-Dihydroxy-3,20-dioxopregn-4-en-21-al.

[e] 11β,17,21-Trihydroxypregna-4,6-diene-3,20-dione.

[f] 17,21-Dihydroxypregna-4-ene-3,11,20-trione.

[g] 17,21-Dihydroxypregn-4-ene-3,20-dione.

▲ (USP 1-May-2020)

PERFORMANCE TESTS

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

SPECIFIC TESTS

Add the following:

▲• **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 *Staphylococcus aureus* and *Pseudomonas aeruginosa*.▲ (USP 1-May-2020)

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.

Change to read:

• **USP Reference Standards ⟨11⟩**

USP Hydrocortisone RS

▲ USP Prednisolone RS▲ (USP 1-May-2020)

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

Topic/Question	Contact	Expert Committee
HYDROCORTISONE GEL	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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