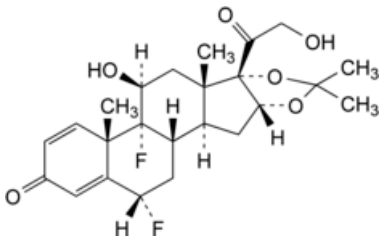
Edition: BP 2025 (Ph. Eur. 11.6 update)

# Fluocinolone Acetonide

General Notices

*(Ph. Eur. monograph 0494)*



$C_{24}H_{30}F_2O_6$ 452.5 *67-73-2*

**Action and use**

Glucocorticoid.

**Preparations**

Fluocinolone Cream

Fluocinolone Ointment

Ph Eur

## DEFINITION

6α,9-Difluoro-11β,21-dihydroxy-16α,17-(1-methylethylidenedioxy)pregna-1,4-diene-3,20-dione.

**Content**

97.5 per cent to 102.0 per cent (dried substance).

## CHARACTERS

**Appearance**

White or almost white, crystalline powder.

**Solubility**

Practically insoluble in water, soluble in acetone and in anhydrous ethanol, practically insoluble in heptane.

It shows polymorphism (*5.9*).

## IDENTIFICATION

A. Infrared absorption spectrophotometry (2.2.24).

*Comparison* *fluocinolone acetonide CRS*.

If the spectra obtained in the solid state show differences, dissolve the substance to be examined and the reference substance separately in *anhydrous ethanol R*, evaporate to dryness and record new spectra using the residues.

B. Examine the chromatograms obtained in the assay.

*Results* The principal peak in the chromatogram obtained with test solution (b) is similar in retention time and size to the principal peak in the chromatogram obtained with reference solution (d).

## TESTS

**Specific optical rotation** (2.2.7)

+ 100 to + 104 (dried substance).

Dissolve 0.100 g in *anhydrous ethanol R* and dilute to 10.0 mL with the same solvent.

**Related substances**

Liquid chromatography (2.2.29). *Carry out the test protected from lightand prepare the solutions immediately before use.*

*Solvent mixture* *acetonitrile R*, *water R* (20:80 *V/V*).

*Buffer solution* Dissolve 5.68 g of *anhydrous disodium hydrogen phosphate R* and 3.63 g of *potassium dihydrogen phosphate R* in *water R* and dilute to 1000.0 mL with the same solvent.

*Test solution (a)* Dissolve 20.0 mg of the substance to be examined in 20 mL of *acetonitrile R* and dilute to 100.0 mL with *water R*.

*Test solution (b)* Dilute 1.0 mL of test solution (a) to 10.0 mL with the solvent mixture.

*Reference solution (a)* Dissolve 2 mg of *fluocinolone acetonide for system suitability CRS* (containing impurities H, J and K) in 2 mL of *acetonitrile R* and dilute to 10.0 mL with *water R*.

*Reference solution (b)* Dissolve 2 mg of *fluocinolone acetonide for peak identification CRS* (containing impurities D and I) in 2 mL of *acetonitrile R* and dilute to 10.0 mL with *water R*.

*Reference solution (c)* Dilute 1.0 mL of test solution (a) to 100.0 mL with the solvent mixture. Dilute 1.0 mL of this solution to 10.0 mL with the solvent mixture.

*Reference solution (d)* Dissolve 20.0 mg of *fluocinolone acetonide CRS* in 20 mL of *acetonitrile R* and dilute to 100.0 mL with *water R*. Dilute 1.0 mL of the solution to 10.0 mL with the solvent mixture.

*Column*:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

— *stationary phase*: *end-capped octadecylsilyl silica gel for chromatography R* (5 µm).

*Mobile phase*:

— *mobile phase A*: *acetonitrile R*, buffer solution (28:72 *V/V*);

— *mobile phase B*: *water R*, *acetonitrile R* (40:60 *V/V*);

| Time (min) | Mobile phase A (per cent *V/V*) | Mobile phase B (per cent *V/V*) |
|---|---|---|
| 0 - 2 | 100 | 0 |
| 2 - 42 | 100 → 0 | 0 → 100 |

*Flow rate* 1.0 mL/min.

*Detection* Spectrophotometer at 238 nm.

*Injection* 40 µL of test solution (a) and reference solutions (a), (b) and (c).

*Identification of impurities* Use the chromatogram supplied with *fluocinolone acetonide for system suitability CRS* and the chromatogram obtained with reference solution (a) to identify the peaks due to impurities H, J and K; use the chromatogram supplied with *fluocinolone acetonide for peak identification CRS* and the chromatogram obtained with reference solution (b) to identify the peaks due to impurities D and I.

*Relative retention* With reference to fluocinolone acetonide (retention time = about 18 min): impurity D = about 0.8; impurity H = about 0.90; impurity I = about 0.94; impurity J = about 1.05; impurity K = about 1.2.

*System suitability* Reference solution (a):

— *peak-to-valley ratio*: minimum 5.0, where $H_p$ = height above the baseline of the peak due to impurity J and $H_v$ = height above the baseline of the lowest point of the curve separating this peak from the peak due to fluocinolone acetonide.

*Calculation of percentage contents*:

— *correction factor*: multiply the peak area of impurity K by 1.3;

— for each impurity, use the concentration of fluocinolone acetonide in reference solution (c).

*Limits*:

— *impurity K*: maximum 0.3 per cent;

— *impurities D, J*: for each impurity, maximum 0.2 per cent;

— *impurities H, I*: for each impurity, maximum 0.15 per cent;

— *unspecified impurities*: for each impurity, maximum 0.10 per cent;

— *total*: maximum 0.7 per cent;

— *reporting threshold*: 0.05 per cent.

**Loss on drying** (*2.2.32*)

Maximum 1.0 per cent, determined on 1.000 g by drying in an oven at 105 °C for 3 h.

## ASSAY

Liquid chromatography (*2.2.29*) as described in the test for related substances with the following modification.

*Injection* 20 µL of test solution (b) and reference solution (d).

Calculate the percentage content of $C_{24}H_{30}F_2O_6$ taking into account the assigned content of *fluocinolone acetonide CRS*.

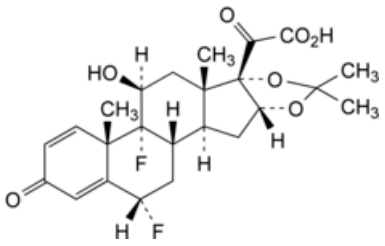
## STORAGE

Protected from light.

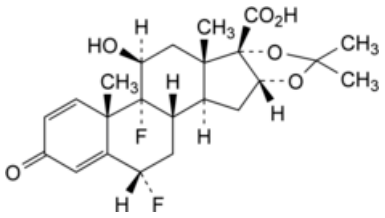
## IMPURITIES

*Specified impurities* D, H, I, J, K.

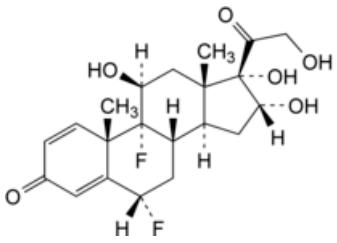
*Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical use (2034). It is therefore not necessary to identify these impurities for demonstration of compliance. See also 5.10. Control of impurities in substances for pharmaceutical use)* A, B, C, E, F, G, L, M.



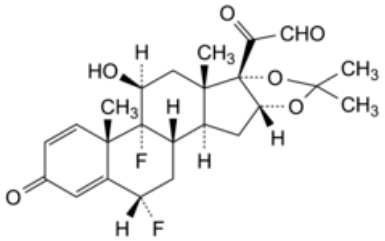
A. 6α,9-difluoro-11β-hydroxy-16α,17-(1-methylethylidenedioxy)-3,20-dioxopregna-1,4-dien-21-oic acid,



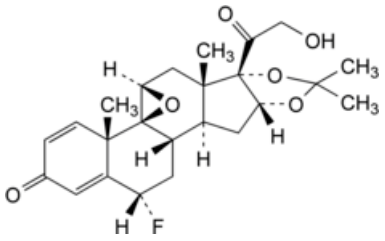
B. 6α,9-difluoro-11β-hydroxy-16α,17-(1-methylethylidenedioxy)-3-oxoandrosta-1,4-diene-17β-carboxylic acid,



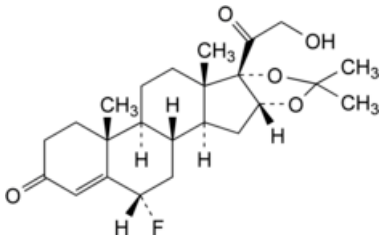
C. 6α,9-difluoro-11β,16α,17,21-tetrahydroxypregna-1,4-diene-3,20-dione (fluocinolone),



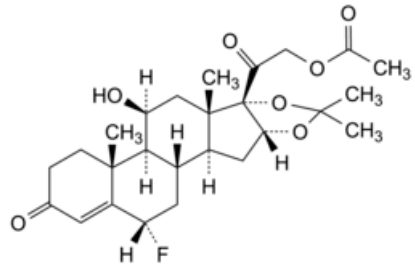
D. 6α,9-difluoro-11β-hydroxy-16α,17-(1-methylethylidenedioxy)-3,20-dioxopregna-1,4-dien-21-al,



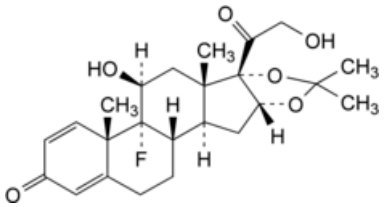
E. 9,11β-epoxy-6α-fluoro-21-hydroxy-16α,17-(1-methylethylidenedioxy)-9β-pregna-1,4-diene-3,20-dione,



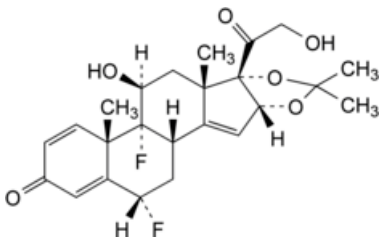
F. 6α-fluoro-21-hydroxy-16α,17-(1-methylethylidenedioxy)pregn-4-ene-3,20-dione,



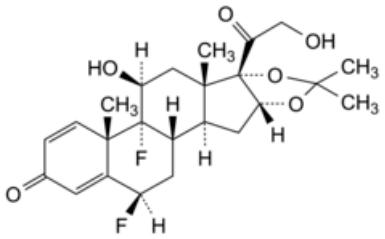
G. 6α-fluoro-11β-hydroxy-16α,17-(1-methylethylidenedioxy)-3,20-dioxopregn-4-en-21-yl acetate,



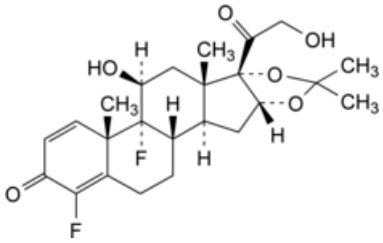
H. 9-fluoro-11β,21-dihydroxy-16α,17-(1-methylethylidenedioxy)pregna-1,4-diene-3,20-dione,



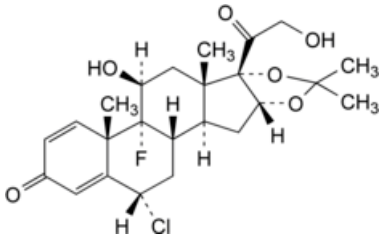
I. 6α,9-difluoro-11β,21-dihydroxy-16α,17-(1-methylethylidenedioxy)pregna-1,4,14-triene-3,20-dione,



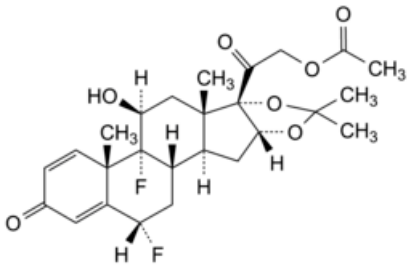
J. 6β,9-difluoro-11β,21-dihydroxy-16α,17-(1-methylethylidenedioxy)pregna-1,4-diene-3,20-dione,



K. 4,9-difluoro-11β,21-dihydroxy-16α,17-(1-methylethylidenedioxy)pregna-1,4-diene-3,20-dione,



L. 6α-chloro-9-fluoro-11β,21-dihydroxy-16α,17-(1-methylethylidenedioxy)pregna-1,4-diene-3,20-dione,



M. 6α,9-difluoro-11β-hydroxy-16α,17-(1-methylethylidenedioxy)-3,20-dioxopregna-1,4-dien-21-yl acetate.

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