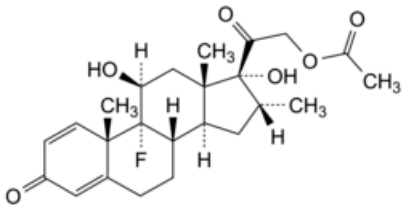
Edition: BP 2025 (Ph. Eur. 11.6 update)

Dexamethasone Acetate

General Notices

(Ph. Eur. monograph 0548)



$C_{24}H_{31}FO_6$ 434.5 *1177-87-3*

Action and use

Glucocorticoid.

Ph Eur

DEFINITION

9-Fluoro-11β,17-dihydroxy-16α-methyl-3,20-dioxopregna-1,4-dien-21-yl acetate.

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, freely soluble in ethanol (96 per cent), slightly soluble in methylene chloride.

It shows polymorphism (*5.9*).

IDENTIFICATION

First identification: A, D.

Second identification: B, C.

A. Infrared absorption spectrophotometry (2.2.24).

Comparison *dexamethasone acetate CRS*.

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

B. Thin-layer chromatography (2.2.27).

Test solution Dissolve 10 mg of the substance to be examined in the mobile phase and dilute to 10.0 mL with the mobile phase.

Reference solution Dissolve 10 mg of *dexamethasone acetate CRS* in the mobile phase and dilute to 10.0 mL with the mobile phase.

Plate *TLC silica gel F_{254} plate R*.

Mobile phase *methanol R*, *methylene chloride R* (10:90 *V/V*).

Application 5 µL.

Development Over 3/4 of the plate.

Drying In air.

Detection Spray with a solution prepared as follows: dissolve 0.25 g of *2,4-dihydroxybenzaldehyde R* in *glacial acetic acid R*, dilute to 50 mL with the same solvent and add a mixture of 12.5 mL of *sulfuric acid R* and 37.5 mL of *glacial acetic acid R*; heat at 90 °C for 35 min or until the spots appear, allow to cool and examine in daylight and in ultraviolet light at 365 nm.

Results The principal spot in the chromatogram obtained with the test solution is similar in position, colour and size to the principal spot in the chromatogram obtained with the reference solution.

C. Add about 2 mg to 2 mL of *sulfuric acid R* and shake to dissolve. Within 5 min, a faint reddish-brown colour develops. Add this solution to 10 mL of *water R* and mix. The colour is discharged and a clear solution remains.
D. 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 (e).

TESTS

Specific optical rotation (2.2.7)

+ 94 to + 99 (dried substance).

Dissolve 0.250 g in *anhydrous ethanol R* and dilute to 25.0 mL with the same solvent.

Related substances

Liquid chromatography (2.2.29). *Carry out the test protected from light.*

Test solution (a) Dissolve 25.0 mg of the substance to be examined in about 4 mL of *acetonitrile R* and dilute to 10.0 mL with *water R*.

Test solution (b) Dilute 1.0 mL of test solution (a) to 5.0 mL with the mobile phase.

Reference solution (a) Dissolve 2 mg of *dexamethasone CRS* (impurity A) and 2 mg of *betamethasone acetate CRS* (impurity D) in the mobile phase, using sonication for about 10 min, and dilute to 100 mL with the mobile phase. Mix 1 mL of this solution and 6 mL of test solution (a) and dilute to 10 mL with the mobile phase.

Reference solution (b) Dilute 1.0 mL of test solution (a) to 100.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 10.0 mL with the mobile phase.

Reference solution (c) Dissolve the contents of a vial of *dexamethasone acetate impurity E CRS* in 1 mL of the mobile phase.

Reference solution (d) Dissolve 5 mg of *dexamethasone acetate for peak identification CRS* (containing impurity I) in about 0.8 mL of *acetonitrile R* and dilute to 2 mL with *water R*.

Reference solution (e) Dissolve 25.0 mg of *dexamethasone acetate CRS* in about 4 mL of *acetonitrile R* and dilute to 10.0 mL with *water R*. Dilute 1.0 mL of the solution to 5.0 mL with the mobile phase.

Column:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

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

Mobile phase Mix 380 mL of *acetonitrile R* and 550 mL of *water for chromatography R* and allow to equilibrate; dilute to 1000 mL with *water for chromatography R* and mix.

Flow rate 1 mL/min.

Detection Spectrophotometer at 254 nm.

Injection 20 µL of test solution (a) and reference solutions (a), (b), (c) and (d).

Run time 2.5 times the retention time of dexamethasone acetate.

Identification of impurities Use the chromatogram obtained with reference solution (a) to identify the peaks due to impurities A and D; use the chromatogram obtained with reference solution (c) to identify the peak due to impurity E; use the chromatogram supplied with *dexamethasone acetate for peak identification CRS* and the chromatogram obtained with reference solution (d) to identify the peak due to impurity I.

Relative retention With reference to dexamethasone acetate (retention time = about 22 min): impurity A = about 0.4; impurity D = about 0.9; impurity E = about 1.2; impurity I = about 1.4.

System suitability Reference solution (a):

— *resolution*: minimum 3.3 between the peaks due to impurity D and dexamethasone acetate.

Limits:

— *impurity I*: not more than 4 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.4 per cent);

— *impurity D*: not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.3 per cent);

— *impurities A, E*: for each impurity, not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent);

— *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.10 per cent);

— *total*: not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent);

— *disregard limit*: 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent).

Loss on drying (*2.2.32*)

Maximum 0.5 per cent, determined on 1.000 g by drying *in vacuo* at 105 °C.

ASSAY

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

Mobile phase *acetonitrile R*, *water for chromatography R* (45:55 *V/V*).

Injection Test solution (b) and reference solution (e).

Run time 1.5 times the retention time of dexamethasone acetate.

Retention time Dexamethasone acetate = about 13 min.

Calculate the percentage content of $C_{24}H_{31}FO_6$ taking into account the assigned content of *dexamethasone acetate CRS*.

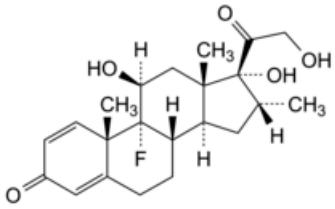
STORAGE

Protected from light.

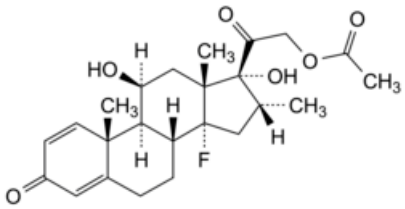
IMPURITIES

Specified impurities *A, D, E, I*.

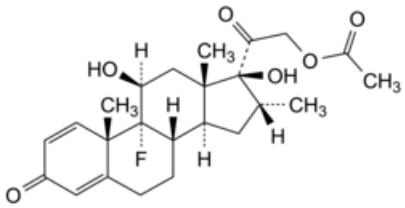
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical 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) *B, C, F, G, H*.



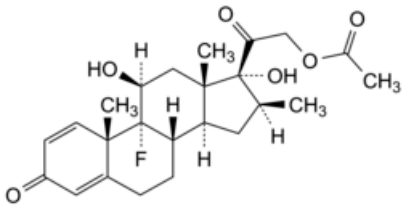
A. 9-fluoro-11β,17,21-trihydroxy-16α-methylpregna-1,4-diene-3,20-dione (dexamethasone),



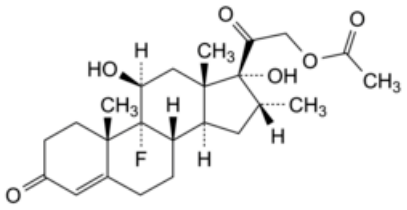
B. 14-fluoro-11β,17-dihydroxy-16α-methyl-3,20-dioxopregna-1,4-dien-21-yl acetate,



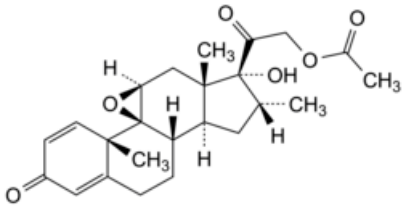
C. 9-fluoro-11β,17-dihydroxy-16α-methyl-3,20-dioxo-17α-pregna-1,4-dien-21-yl acetate,



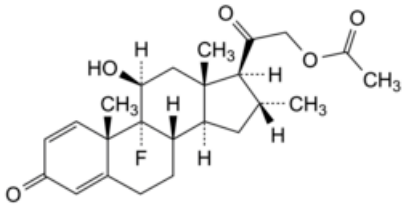
D. 9-fluoro-11β,17-dihydroxy-16β-methyl-3,20-dioxopregna-1,4-dien-21-yl acetate (betamethasone acetate),



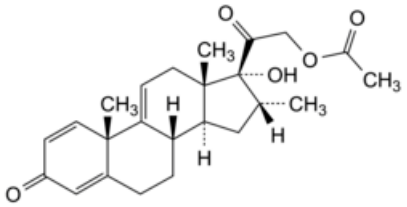
E. 9-fluoro-11β,17-dihydroxy-16α-methyl-3,20-dioxopregn-4-en-21-yl acetate,



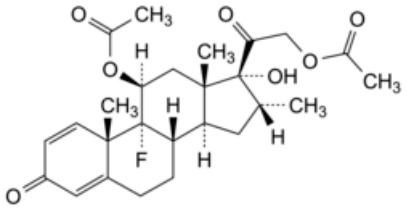
F. 9,11β-epoxy-17-hydroxy-16α-methyl-3,20-dioxo-9β-pregna-1,4-dien-21-yl acetate,



G. 9-fluoro-11β-hydroxy-16α-methyl-3,20-dioxopregna-1,4-dien-21-yl acetate,



H. 17-hydroxy-16α-methyl-3,20-dioxopregna-1,4,9(11)-trien-21-yl acetate,



I. 9-fluoro-17-hydroxy-16α-methyl-3,20-dioxopregna-1,4-diene-11β,21-diyl diacetate (dexamethasone 11,21-diacetate).

Ph Eur