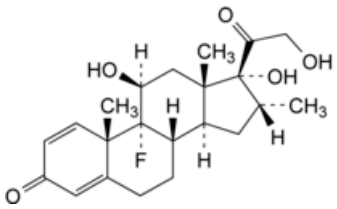
Edition: BP 2025 (Ph. Eur. 11.6 update)

Dexamethasone

General Notices

(Ph. Eur. monograph 0388)



$C_{22}H_{29}FO_5$ 392.5 *50-02-2*

Action and use

Glucocorticoid.

Preparations

Dexamethasone Eye Drops, Suspension

Dexamethasone and Neomycin Ear Spray

Dexamethasone Tablets

Tobramycin and Dexamethasone Eye Drops, Suspension

Ph Eur

DEFINITION

9-Fluoro-11β,17,21-trihydroxy-16α-methylpregna-1,4-diene-3,20-dione.

Content

97.0 per cent to 103.0 per cent (dried substance).

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Practically insoluble in water, sparingly soluble in anhydrous ethanol, slightly soluble in methylene chloride.

IDENTIFICATION

First identification: A, B.

Second identification: B, C.

A. Infrared absorption spectrophotometry (2.2.24).

Comparison dexamethasone CRS.

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 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.

TESTS

Specific optical rotation (2.2.7)

+ 86 to + 92 (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 Dissolve 25.0 mg of the substance to be examined in 1.5 mL of acetonitrile R and add 5 mL of mobile phase A. Sonicate until dissolution is complete and dilute to 10.0 mL with mobile phase A.

Reference solution (a) Dissolve 5 mg of dexamethasone for system suitability CRS (containing impurities B, F and G) in 0.5 mL of acetonitrile R and add 1 mL of mobile phase A. Sonicate until dissolution is complete and dilute to 2 mL with mobile phase A.

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

Reference solution (c) Dissolve 5 mg of *dexamethasone for peak identification CRS* (containing impurities J and K) in 0.5 mL of *acetonitrile R* and add 1 mL of mobile phase A. Sonicate until dissolution is complete and dilute to 2 mL with mobile phase A.

Column:

— *size*: *l* = 0.15 m, Ø = 4.6 mm;

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

— *temperature*: 45 °C.

Mobile phase:

— *mobile phase A*: mix 250 mL of *acetonitrile R* and 700 mL of *water for chromatography R* and allow to equilibrate; dilute to 1000 mL with *water for chromatography R* and mix;

— *mobile phase B*: *acetonitrile R*;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 15	100	0
15 - 40	100 → 0	0 → 100

Flow rate 1.2 mL/min.

Detection Spectrophotometer at 254 nm.

Injection 20 µL; inject mobile phase A as a blank.

Identification of impurities Use the chromatogram supplied with *dexamethasone for system suitability CRS* and the chromatogram obtained with reference solution (a) to identify the peaks due to impurities B, F and G; use the chromatogram supplied with *dexamethasone for peak identification CRS* and the chromatogram obtained with reference solution (c) to identify the peaks due to impurities J and K.

Relative retention With reference to dexamethasone (retention time = about 15 min): impurity J = about 0.90; impurity B = about 0.94; impurity K = about 1.3; impurity F = about 1.5; impurity G = about 1.7.

System suitability Reference solution (a):

— *peak-to-valley ratio*: minimum 2.0, where H_p = height above the baseline of the peak due to impurity B and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to dexamethasone.

Limits:

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

— *impurities B, F, J, K*: for each impurity, not more than 1.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.15 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 0.500 g by drying in an oven at 105 °C.

ASSAY

Dissolve 0.100 g in *ethanol (96 per cent) R* and dilute to 100.0 mL with the same solvent. Dilute 2.0 mL of the solution to 100.0 mL with *ethanol (96 per cent) R*. Measure the absorbance (*2.2.25*) at the absorption maximum at 238.5 nm.

Calculate the content of $C_{22}H_{29}FO_5$ taking the specific absorbance to be 394.

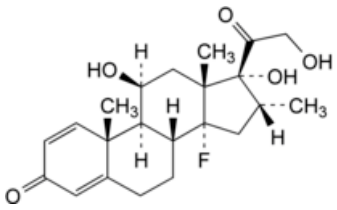
STORAGE

Protected from light.

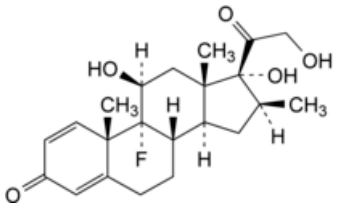
IMPURITIES

Specified impurities *B, F, G, J, K.*

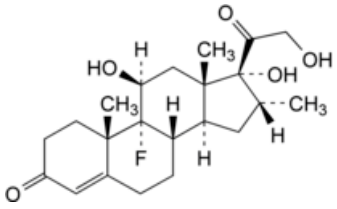
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical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



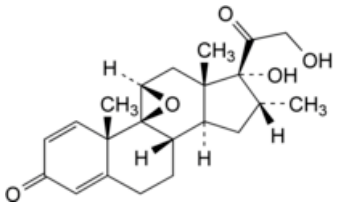
A. 14-fluoro-11β,17,21-trihydroxy-16α-methylpregna-1,4-diene-3,20-dione,



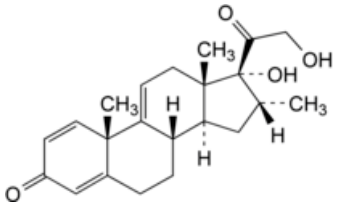
B. 9-fluoro-11β,17,21-trihydroxy-16β-methylpregna-1,4-diene-3,20-dione (betamethasone),



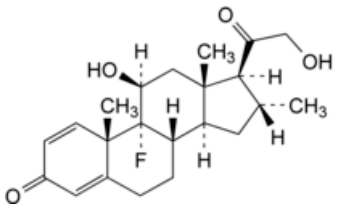
C. 9-fluoro-11β,17,21-trihydroxy-16α-methylpregn-4-ene-3,20-dione,



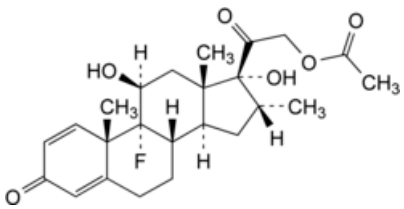
D. 9,11β-epoxy-17,21-dihydroxy-16α-methyl-9β-pregna-1,4-diene-3,20-dione,



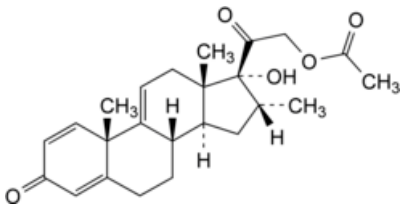
E. 17,21-dihydroxy-16α-methylpregna-1,4,9(11)-triene-3,20-dione,



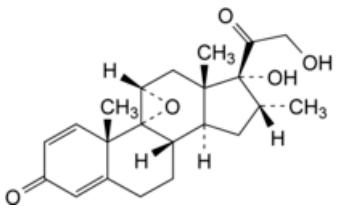
F. 9-fluoro-11β,21-dihydroxy-16α-methylpregna-1,4-diene-3,20-dione,



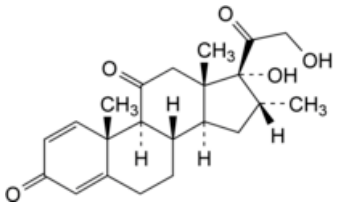
G. 9-fluoro-11β,17-dihydroxy-16α-methyl-3,20-dioxopregna-1,4-dien-21-yl acetate (dexamethasone acetate),



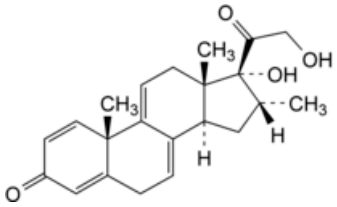
H. 17-hydroxy-16α-methyl-3,20-dioxopregna-1,4,9(11)-trien-21-yl acetate,



I. 9,11α-epoxy-17,21-dihydroxy-16α-methylpregna-1,4-diene-3,20-dione,



J. 17,21-dihydroxy-16α-methylpregna-1,4-diene-3,11,20-trione,



K. 17,21-dihydroxy-16α-methylpregna-1,4,7,9(11)-tetraene-3,20-dione.

Ph Eur