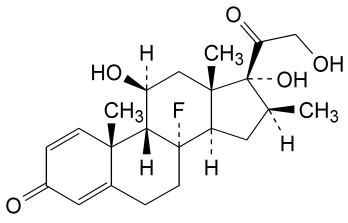
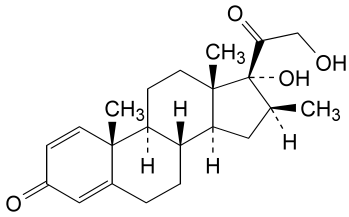


I. 8-fluoro-11β,17,21-trihydroxy-16β-methyl-8α,9β-pregna-1,4-diene-3,20-dione,

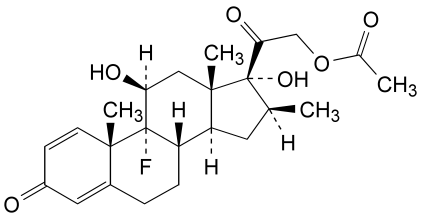


J. 17,21-dihydroxy-16β-methylpregna-1,4-diene-3,20-dione.

**01/2008:0975**

# BETAMETHASONE ACETATE

## Betamethasoni acetas



$C_{24}H_{31}FO_6$ $M_r$ 434.5
[987-24-6]

DEFINITION

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

*Content*: 97.0 per cent to 103.0 per cent (anhydrous substance).

CHARACTERS

*Appearance*: white or almost white, crystalline powder.

*Solubility*: practically insoluble in water, freely soluble in acetone, soluble in ethanol (96 per cent) and in methylene chloride.

It shows polymorphism (*5.9*).

IDENTIFICATION

*First identification: B, C.*

*Second identification: A, C, D, E, F.*

A. Dissolve 10.0 mg in *anhydrous ethanol R* and dilute to 100.0 ml with the same solvent. Place 2.0 ml of this solution in a ground-glass-stoppered tube, add 10.0 ml of *phenylhydrazine-sulphuric acid solution R*, mix and heat in a water-bath at 60 °C for 20 min. Cool immediately. The absorbance (*2.2.25*) measured at 419 nm is not greater than 0.10.

B. Infrared absorption spectrophotometry (*2.2.24*).

*Comparison*: *betamethasone acetate CRS.*

If the spectra obtained in the solid state show differences, dissolve the substance to be examined and the reference substance separately in the minimum volume of *methanol R*, evaporate to dryness on a water-bath and record new spectra using the residues.

C. Thin-layer chromatography (*2.2.27*).

*Solvent mixture*: *methanol R, methylene chloride R* (1:9 *V/V*).

*Test solution.* Dissolve 10 mg of the substance to be examined in the solvent mixture and dilute to 10 ml with the solvent mixture.

*Reference solution (a).* Dissolve 20 mg of *betamethasone acetate CRS* in the solvent mixture and dilute to 20 ml with the solvent mixture.

*Reference solution (b).* Dissolve 10 mg of *prednisolone acetate CRS* in reference solution (a) and dilute to 10 ml with reference solution (a).

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

*Mobile phase*: add a mixture of 1.2 volumes of *water R* and 8 volumes of *methanol R* to a mixture of 15 volumes of *ether R* and 77 volumes of *methylene chloride R.*

*Application*: 5 µl.

*Development*: over a path of 15 cm.

*Drying*: in air.

*Detection A*: examine in ultraviolet light at 254 nm.

*Results A*: the principal spot in the chromatogram obtained with the test solution is similar in position and size to the principal spot in the chromatogram obtained with reference solution (a).

*Detection B*: spray with *alcoholic solution of sulphuric acid R*. Heat at 120 °C for 10 min or until the spots appear. Allow to cool. Examine in daylight and in ultraviolet light at 365 nm.

*Results B*: the principal spot in the chromatogram obtained with the test solution is similar in position, colour in daylight, fluorescence in ultraviolet light at 365 nm and size to the principal spot in the chromatogram obtained with reference solution (a).

*System suitability*: reference solution (b):

– the chromatogram shows 2 clearly separated spots.

D. Add about 2 mg to 2 ml of *sulphuric acid R* and shake to dissolve. Within 5 min, a deep reddish-brown colour develops. Add this solution to 10 ml of *water R* and mix. The colour is discharged and a clear solution remains.

E. Mix about 5 mg with 45 mg of *heavy magnesium oxide R* and ignite in a crucible until an almost white residue is obtained (usually less than 5 min). Allow to cool, add 1 ml of *water R*, 0.05 ml of *phenolphthalein solution R1* and about 1 ml of *dilute hydrochloric acid R* to render the solution colourless. Filter. To a freshly prepared mixture of 0.1 ml of *alizarin S solution R* and 0.1 ml of *zirconyl nitrate solution R*, add 1.0 ml of the filtrate. Mix, allow to stand for 5 min and compare the colour of the solution with that of a blank prepared in the same manner. The test solution is yellow and the blank is red.

F. About 10 mg gives the reaction of acetyl (*2.3.1*).

TESTS

**Specific optical rotation** (*2.2.7*): + 120 to + 128 (anhydrous substance).

Dissolve 0.250 g in *dioxan R* and dilute to 25.0 ml with the same solvent.

**Related substances**. Liquid chromatography (*2.2.29*).

*Test solution.* Dissolve 25.0 mg of the substance to be examined in 4 ml of *acetonitrile R* and dilute to 10.0 ml with the same solvent.

*Reference solution (a).* Dissolve 2 mg of *betamethasone acetate CRS* and 2 mg of *dexamethasone acetate CRS* (impurity B) in the mobile phase, then dilute to 100.0 ml with the mobile phase.

*Reference solution (b).* Dilute 1.0 ml of the test solution to 100.0 ml with the mobile phase.

*Column*:

– *size*: *l* = 0.25 m, Ø = 4.6 mm;
– *stationary phase*: *octadecylsilyl silica gel for chromatography R* (5 µm).

*Mobile phase*: in a 1000 ml volumetric flask mix 380 ml of *acetonitrile R* with 550 ml of *water R* and allow to equilibrate; dilute to 1000 ml with *water R* and mix again.

*Flow rate*: 1 ml/min.

*Detection*: spectrophotometer at 254 nm.

*Equilibration*: with the mobile phase for about 30 min.

*Injection*: 20 µl.

*Run time*: 2.5 times the retention time of betamethasone acetate.

*Retention time*: betamethasone acetate = about 19 min; impurity B = about 22 min.

*System suitability*: reference solution (a):

– *resolution*: minimum 3.3 between the peaks due to betamethasone acetate and impurity B; if necessary, adjust slightly the concentration of acetonitrile in the mobile phase.

*Limits*:

– *impurities A, B, C, D*: for each impurity, not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent);
– *total*: not more than 1.25 times the area of the principal peak in the chromatogram obtained with reference solution (b) (1.25 per cent);
– *disregard limit*: 0.05 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent).

**Water** (*2.5.12*): maximum 4.0 per cent, determined on 0.100 g.

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 this solution to 100.0 ml with *ethanol (96 per cent) R*. Measure the absorbance (*2.2.25*) at the absorption maximum at 240 nm.

Calculate the content of $C_{24}H_{31}FO_6$ taking the specific absorbance to be 350.

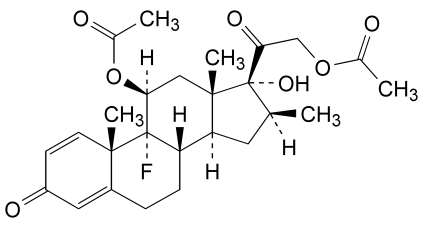
STORAGE

Protected from light.

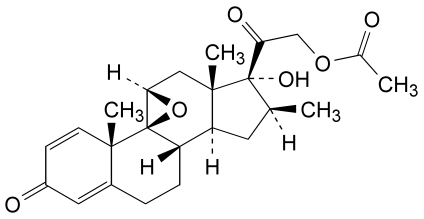
IMPURITIES

*Specified impurities*: *A, B, C, D.*

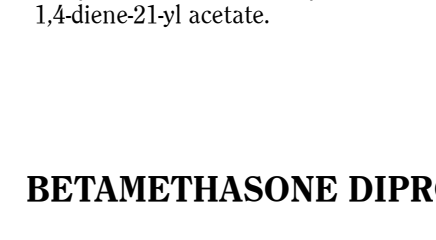
A. betamethasone,



B. dexamethasone acetate,



C. betamethasone 11,21-diacetate,

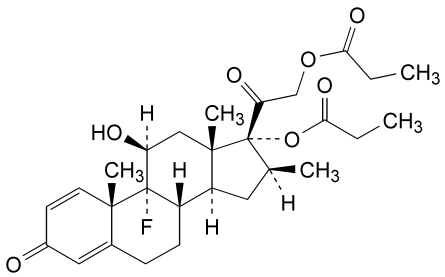


D. 9,11β-epoxy-17-hydroxy-16β-methyl-3,20-dioxo-9β-pregna-1,4-diene-21-yl acetate.

**01/2008:0809**
**corrected 6.0**

# BETAMETHASONE DIPROPIONATE

## Betamethasoni dipropionas



$C_{28}H_{37}FO_7$ $M_r$ 504.6
[5593-20-4]

DEFINITION

9-Fluoro-11β-hydroxy-16β-methyl-3,20-dioxopregna-1,4-diene-17,21-diyl dipropanoate.

*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, freely soluble in acetone and in methylene chloride, sparingly soluble in ethanol (96 per cent).

IDENTIFICATION

*First identification: B, C.*

*Second identification: A, D, E, F.*

A. Dissolve 10.0 mg in *anhydrous ethanol R* and dilute to 100.0 ml with the same solvent. Place 2.0 ml of this solution in a ground-glass-stoppered tube, add 10.0 ml of *phenylhydrazine-sulphuric acid solution R*, mix and heat in a water-bath at 60 °C for 20 min. Cool immediately. The absorbance (*2.2.25*) measured at 419 nm is not more than 0.10.

B. Infrared absorption spectrophotometry (*2.2.24*).
*Comparison*: *betamethasone dipropionate CRS.*

C. Thin-layer chromatography (*2.2.27*).