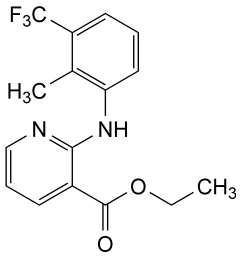
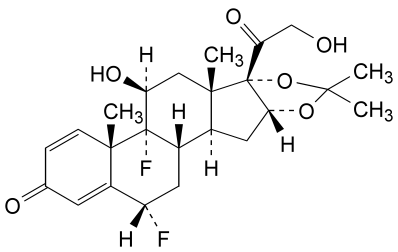


D. ethyl 2-[[2-methyl-3-(trifluoromethyl)phenyl]amino]pyridine-3-carboxylate.

01/2008:0494
corrected 6.0

FLUOCINOLONE ACETONIDE

Fluocinoloni acetonidum



$C_{24}H_{30}F_2O_6$ M_r 452.5
[67-73-2]

DEFINITION

6α,9-Difluoro-11β,21-dihydroxy-16α,17-(1-methylethylidenedioxy)pregna-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, soluble in acetone and in ethanol.

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 *ethanol R*, evaporate to dryness and record new spectra using the residues.

B. Examine the chromatograms obtained in the test for related substances.

Results: the principal peak in the chromatogram obtained with the reference solution (b) is similar in retention time to the peak due to *fluocinolone acetonide CRS* in the chromatogram obtained with the reference solution (a).

TESTS

Specific optical rotation (*2.2.7*): + 100 to + 104 (dried substance).

Dissolve 0.100 g in *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 light.*

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

Reference solution (a). Dissolve 2.5 mg of *fluocinolone acetonide CRS* and 2.5 mg of *triamcinolone acetonide R* in 45 ml of *acetonitrile R* and dilute to 100.0 ml with *water R*.

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

Column:

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

Mobile phase: mix 450 ml of *acetonitrile R* with 500 ml of *water R* and allow to equilibrate; adjust the volume to 1000.0 ml with *water R* and mix again.

Flow rate: 1 ml/min.

Detection: spectrophotometer at 238 nm.

Injection: 20 µl.

Run time: 4 times the retention time of fluocinolone acetonide.

Retention times: triamcinolone acetonide = about 8.5 min; fluocinolone acetonide = about 10 min.

System suitability:

– *resolution*: minimum of 3.0 between the peaks due to triamcinolone acetonide and fluocinolone acetonide in the chromatogram obtained with reference solution (a).

Limits:

– *any impurity*: not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (1 per cent) and not more than 1 such peak has an area greater than half the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent),
– *total*: not more than 2.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (2.5 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).

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

Protect the solutions from light throughout the assay.

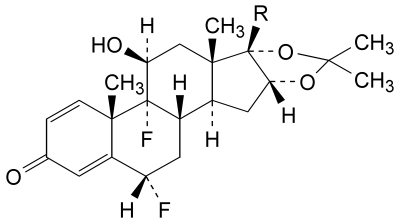
Dissolve 50.0 mg in *alcohol R* and dilute to 50.0 ml with the same solvent. Dilute 2.0 ml of this solution to 100.0 ml with *alcohol R*. Measure the absorbance (*2.2.25*) at the maximum at 238 nm.

Calculate the content of $C_{24}H_{30}F_2O_6$ taking the specific absorbance to be 355.

STORAGE

Protected from light.

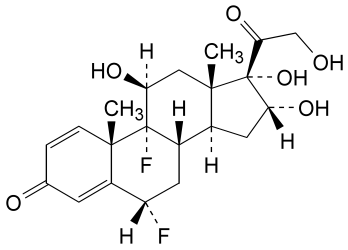
IMPURITIES



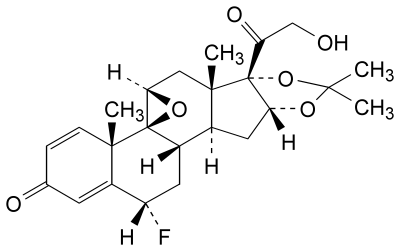
A. R = CO-CO_2H: 6α,9-difluoro-11β-hydroxy-16α,17-(1-methylethylidenedioxy)-3,20-dioxopregna-1,4-dien-21-oic acid,

B. R = CO_2H: 6α,9-difluoro-11β-hydroxy-16α,17-(1-methylethylidenedioxy)-3-oxoandrosta-1,4-diene-17β-carboxylic acid,

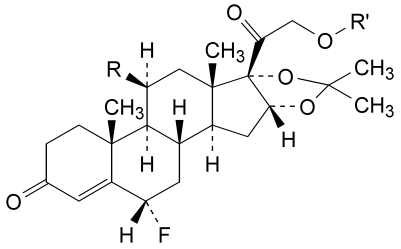
D. R = CO-CH=O: 6α,9-difluoro-11β-hydroxy-16α,17-(1-methylethylidenedioxy)-3,20-dioxopregna-1,4-dien-21-al,



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



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



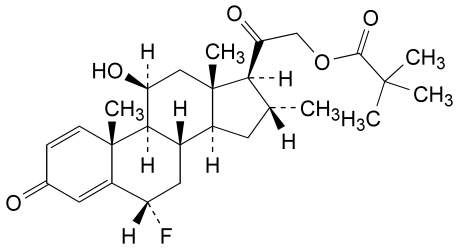
F. R = R′ = H: 6α-fluoro-21-hydroxy-16α,17-(1-methylethylidenedioxy)pregn-4-ene-3,20-dione,

G. R = OH, R′ = CO-CH_3: 6α-fluoro-11β-hydroxy-16α,17-(1-methylethylidenedioxy)-3,20-dioxopregn-4-en-21-yl acetate.

01/2008:1212
corrected 6.0

FLUOCORTOLONE PIVALATE

Fluocortoloni pivalas



$C_{27}H_{37}FO_5$ M_r 460.6
[29205-06-9]

DEFINITION

6α-Fluoro-11β-hydroxy-16α-methyl-3,20-dioxopregna-1,4-dien-21-yl 2,2-dimethylpropanoate.

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 methylene chloride and in dioxan, sparingly soluble in ethanol (96 per cent).

IDENTIFICATION

First identification: A, B.

Second identification: B, C, D.

A. Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *fluocortolone pivalate CRS.*

B. 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 *fluocortolone pivalate CRS* in the solvent mixture and dilute to 20 ml with the solvent mixture.

Reference solution (b). Dissolve 10 mg of *norethisterone 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.