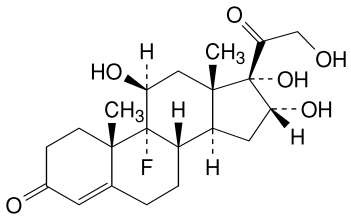
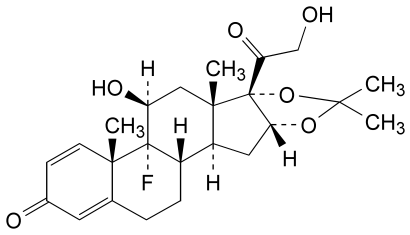


C. 9-fluoro-11β,16α,17,21-tetrahydroxypregn-4-ene-3,20-dione (pretriamcinolone).

01/2008:0533

TRIAMCINOLONE ACETONIDE

Triamcinoloni acetonidum



$C_{24}H_{31}FO_6$ M_r 434.5
[76-25-5]

DEFINITION

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

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, sparingly soluble in ethanol (96 per cent).

It shows polymorphism (*5.9*).

IDENTIFICATION

First identification: A, B.

Second identification: C, D.

A. Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *triamcinolone acetonide 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* and evaporate to dryness. Using the residues, prepare halogen salt discs or mulls in *liquid paraffin R* and record new spectra.

B. Thin-layer chromatography (*2.2.27*). *Prepare the solutions immediately before use and protect from light.*

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

Reference solution (a). Dissolve 20 mg of *triamcinolone acetonide CRS* in *methanol R* and dilute to 20 ml with the same solvent.

Reference solution (b). Dissolve 10 mg of *triamcinolone hexacetonide 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: examine in ultraviolet light at 254 nm, immediately after development.

System suitability: reference solution (b):

– the chromatogram shows 2 clearly separated spots.

Results: 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).

C. Thin-layer chromatography (*2.2.27*). *Prepare the solutions immediately before use and protect from light.*

Test solution (a). Dissolve 10 mg of the substance to be examined in *methanol R* and dilute to 10 ml with the same solvent.

Test solution (b). In a separating funnel, dissolve 10 mg of the substance to be examined in 1.5 ml of *glacial acetic acid R*, add 0.5 ml of a 20 g/l solution of *chromium trioxide R* and allow to stand for 60 min. Add 5 ml of *water R*, 2 ml of *methylene chloride R* and shake vigorously for 2 min. Allow to separate and use the lower layer.

Reference solution (a). Dissolve 10 mg of *triamcinolone acetonide CRS* in *methanol R* and dilute to 10 ml with the same solvent.

Reference solution (b). In a separating funnel, dissolve 10 mg of *triamcinolone acetonide CRS* in 1.5 ml of *glacial acetic acid R*, add 0.5 ml of a 20 g/l solution of *chromium trioxide R* and allow to stand for 60 min. Add 5 ml of *water R*, 2 ml of *methylene chloride R* and shake vigorously for 2 min. Allow to separate and use the lower layer.

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: examine in ultraviolet light at 254 nm, immediately after development.

Results: the principal spot in each of the chromatograms obtained with the test solutions is similar in position and size to the principal spot in the chromatogram obtained with the corresponding reference solution. The principal spot in the chromatograms obtained with test solution (b) and reference solution (b) has an R_F value distinctly higher than that of the principal spot in the chromatograms obtained with test solution (a) and reference solution (a).

D. 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 to that of a blank prepared in the same manner. The test solution is yellow and the blank is red.

TESTS

Specific optical rotation (*2.2.7*): + 100 to + 107 (anhydrous substance).

Dissolve 0.100 g in *dioxan 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 7 ml of *methanol R* and dilute to 10.0 ml with *water R*.

Reference solution (a). Dissolve 2 mg of *triamcinolone acetonide CRS* and 2 mg of *triamcinolone R* (impurity A) in the mobile phase and 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 525 ml of *methanol R* with 400 ml of *water R* and allow to equilibrate; dilute to 1000 ml with *water R* and mix again.

Flow rate: 1.5 ml/min.

Detection: spectrophotometer at 254 nm.

Equilibration: with the mobile phase for about 10 min.

Injection: 20 µl.

Run time: 3.5 times the retention time of triamcinolone acetonide.

Retention time: impurity A = about 5 min; triamcinolone acetonide = about 17 min.

System suitability: reference solution (a):

– *resolution*: minimum 15 between the peaks due to impurity A and triamcinolone acetonide; if necessary, adjust the concentration of methanol in the mobile phase.

Limits:

– *impurity A*: not more than 0.25 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.25 per cent);
– *total*: not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 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).

Water (*2.5.12*): maximum 2.0 per cent, determined on 0.500 g.

ASSAY

Protect the solutions from light throughout the assay.

Dissolve 50.0 mg in *ethanol (96 per cent) R* and dilute to 50.0 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 238.5 nm.

Calculate the content of $C_{24}H_{31}FO_6$ taking the specific absorbance to be 355.

STORAGE

Protected from light.

IMPURITIES

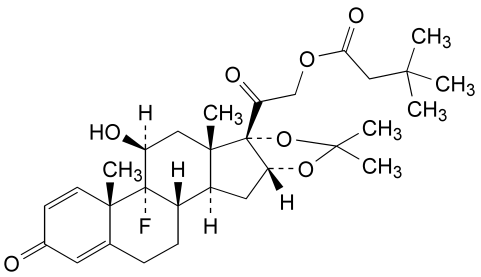
Specified impurities: A.

A. triamcinolone.

01/2008:0867

TRIAMCINOLONE HEXACETONIDE

Triamcinoloni hexacetonidum



$C_{30}H_{41}FO_7$ M_r 532.6
[5611-51-8]

DEFINITION

9-Fluoro-11β-hydroxy-16α,17-(1-methylethylidenedioxy)-3,20-dioxopregna-1,4-diene-21-yl 3,3-dimethylbutanoate.

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, sparingly soluble in anhydrous ethanol and in methanol.

IDENTIFICATION

A. Infrared absorption spectrophotometry (*2.2.24*).
Comparison: *triamcinolone hexacetonide CRS*.

B. Thin-layer chromatography (*2.2.27*). *Prepare the solutions immediately before use and protect from light.*
Test solution. Dissolve 10 mg of the substance to be examined in *methanol R* and dilute to 10 ml with the same solvent.
Reference solution (a). Dissolve 20 mg of *triamcinolone hexacetonide CRS* in *methanol R* and dilute to 20 ml with the same solvent.
Reference solution (b). Dissolve 10 mg of *triamcinolone acetonide 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: examine in ultraviolet light at 254 nm, immediately after development.
System suitability: reference solution (b):
– the chromatogram shows 2 clearly separated spots.