– *total*: not more than 8 times the area of the peak due to dexamethasone isonicotinate in the chromatogram obtained with reference solution (b) (0.8 per cent),
– *disregard limit*: 0.5 times the area of the peak due to dexamethasone isonicotinate 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 102 °C under high vacuum for 4 h.

ASSAY

Dissolve 0.400 g in a mixture of 5 ml of *anhydrous formic acid R* and 50 ml of *glacial acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

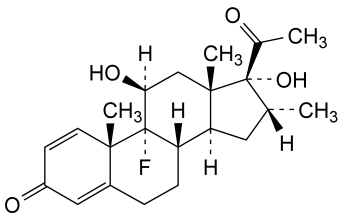
1 ml of *0.1 M perchloric acid* is equivalent to 49.76 mg of $C_{28}H_{32}FNO_6$.

IMPURITIES

Specified impurities: A, B, C.

A. dexamethasone,

B. dexamethasone acetate,

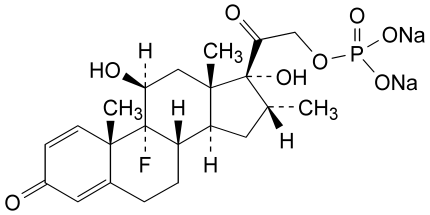


C. 9-fluoro-11,17-dihydroxy-16-methylpregna-1,4-diene-3,20-dione (21-deoxydexamethasone).

01/2008:0549

DEXAMETHASONE SODIUM PHOSPHATE

Dexamethasoni natrii phosphas



$C_{22}H_{28}FNa_2O_8P$ M_r 516.4
[2392-39-4]

DEFINITION

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

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

CHARACTERS

Appearance: white or almost white, very hygroscopic powder.

Solubility: freely soluble in water, slightly soluble in ethanol (96 per cent), practically insoluble 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 5 ml of *water R* and dilute to 100.0 ml with *anhydrous ethanol R*. 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 the absorption maximum at 419 nm is at least 0.20.

B. Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *dexamethasone sodium phosphate 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 *ethanol (96 per cent) R*, evaporate to dryness on a water-bath and record new spectra using the residues.

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

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 *dexamethasone sodium phosphate CRS* in *methanol R* and dilute to 20 ml with the same solvent.

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

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

Mobile phase: *glacial acetic acid R, water R, butanol R* (20:20:60 *V/V/V*).

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 spots which may, however, not be completely separated.

D. Add about 2 mg to 2 ml of *sulphuric acid R* and shake to dissolve. Within 5 min, a faint yellowish-brown colour develops. Add this solution to 10 ml of *water R* and mix. The colour fades 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. To 40 mg add 2 ml of *sulphuric acid R* and heat gently until white fumes are evolved, add *nitric acid R* dropwise, continue the heating until the solution is almost colourless and cool. Add 2 ml of *water R*, heat until white fumes are again evolved, cool, add 10 ml of *water R* and neutralise to *red litmus paper R* with *dilute ammonia R1*. The solution gives reaction (a) of sodium (*2.3.1*) and reaction (b) of phosphates (*2.3.1*).

TESTS

Solution S. Dissolve 1.0 g in *carbon dioxide-free water R* and dilute to 20 ml with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution B_7 (*2.2.2, Method II*).

pH (*2.2.3*): 7.5 to 9.5.

Dilute 1 ml of solution S to 5 ml with *carbon dioxide-free water R*.

Specific optical rotation (*2.2.7*): + 75 to + 83 (anhydrous substance).

Dissolve 0.250 g in *water 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 the mobile phase and dilute to 10.0 ml with the mobile phase.

Reference solution (a). Dissolve 2 mg of *dexamethasone sodium phosphate CRS* and 2 mg of *betamethasone sodium phosphate CRS* 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 250 ml conical flask, weigh 1.360 g of *potassium dihydrogen phosphate R* and 0.600 g of *hexylamine R*, mix and allow to stand for 10 min and then dissolve in 182.5 ml of *water R*; add 67.5 ml of *acetonitrile R*, mix and filter (0.45 µm).

Flow rate: 1 ml/min.

Detection: spectrophotometer at 254 nm.

Equilibration: with the mobile phase for about 45 min.

Injection: 20 µl.

Run time: twice the retention time of dexamethasone sodium phosphate.

Retention time: impurity B = about 12.5 min; dexamethasone sodium phosphate = about 14 min.

System suitability: reference solution (a):

– *resolution*: minimum 2.2 between the peaks due to impurity B and dexamethasone sodium phosphate; if necessary, adjust slightly the concentration of acetonitrile or increase the concentration of water in the mobile phase.

Limits:

– *impurities A, B*: 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 the area of the principal peak in the chromatogram obtained with reference solution (b) (1 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).

Inorganic phosphates: maximum 1 per cent.

Dissolve 50 mg in *water R* and dilute to 100 ml with the same solvent. To 10 ml of this solution add 5 ml of *molybdovanadic reagent R*, mix and allow to stand for 5 min. Any yellow colour in the solution is not more intense than that in a standard prepared at the same time in the same manner using 10 ml of *phosphate standard solution (5 ppm PO_4) R*.

Ethanol. Gas chromatography (*2.2.28*).

Internal standard solution. Dilute 1.0 ml of *propanol R* to 100.0 ml with *water R*.

Test solution. Dissolve 0.50 g of the substance to be examined in 5.0 ml of the internal standard solution and dilute to 10.0 ml with *water R*.

Reference solution. Dilute 1.0 g of *anhydrous ethanol R* to 100.0 ml with *water R*. To 2.0 ml of this solution add 5.0 ml of the internal standard solution and dilute to 10.0 ml with *water R*.

Column:

– *size*: *l* = 1 m, Ø = 3.2 mm;
– *stationary phase*: *ethylvinylbenzene-divinylbenzene copolymer R1* (150-180 µm).

Carrier gas: *nitrogen for chromatography R*.

Flow rate: 30 ml/min.

Temperature:

– *column*: 150 °C;
– *injection port*: 250 °C;
– *detector*: 280 °C.

Detection: flame ionisation.

Injection: 2 µl.

Limit:

– *ethanol*: maximum 3.0 per cent *m/m*.

Ethanol and water: maximum 13.0 per cent *m/m* for the sum of the percentage contents.

Determine the water content using 0.200 g (*2.5.12*). Add the percentage content of water and the percentage content of ethanol obtained in the test for ethanol.

ASSAY

Dissolve 0.100 g in *water R* and dilute to 100.0 ml with the same solvent. Dilute 10.0 ml of this solution to 500.0 ml with *water R*. Measure the absorbance (*2.2.25*) at the absorption maximum at 241.5 nm.

Calculate the content of $C_{22}H_{28}FNa_2O_8P$ taking the specific absorbance to be 303.

STORAGE

In an airtight container, protected from light.

IMPURITIES

Specified impurities: A, B.

A. dexamethasone,

B. betamethasone sodium phosphate.