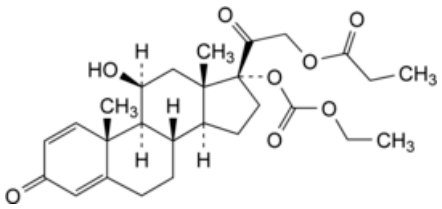
Edition: BP 2025 (Ph. Eur. 11.6 update)

Prednicarbate

General Notices

(Ph. Eur. monograph 1467)



$C_{27}H_{36}O_8$ 488.6 *73771-04-7*

Action and use

Glucocorticoid.

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DEFINITION

11β-Hydroxy-3,20-dioxopregna-1,4-diene-17,21-diyl 17-(ethyl carbonate) 21-propanoate.

Content

97.0 per cent to 102.0 per cent (dried substance).

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Practically insoluble in water, freely soluble in acetone and in ethanol (96 per cent), sparingly soluble in propylene glycol.

It shows polymorphism (*5.9*).

IDENTIFICATION

First identification: A.

Second identification: B.

A. Infrared absorption spectrophotometry (2.2.24).

Comparison prednicarbate 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.

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 prednicarbate 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; the volume may be adapted based on the type of plate used.

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 the plate 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.

TESTS

Specific optical rotation (2.2.7)

+ 60 to + 66 (dried substance).

Dissolve 0.250 g in ethanol (96 per cent) R and dilute to 25.0 mL with the same solvent.

Related substances

Liquid chromatography (2.2.29). *Prepare the solutions immediately before use.*

Test solution Dissolve 30.0 mg of the substance to be examined in the mobile phase and dilute to 50.0 mL with the mobile phase.

Reference solution (a) Dissolve 3 mg of prednicarbate for system suitability A CRS (containing impurities B, C, D, E and F) in the mobile phase and dilute to 5 mL with the mobile phase.

Reference solution (b) Dissolve 3 mg of prednicarbate for peak identification CRS (containing impurity G) in the mobile phase and dilute to 5 mL with the mobile phase.

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

Reference solution (d) Dissolve 30.0 mg of prednicarbate CRS in the mobile phase and dilute to 50.0 mL with the mobile phase.

Column:

— *size*: *l* = 0.125 m, Ø = 4 mm;

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

Mobile phase *acetonitrile for chromatography R*, *water for chromatography R* (50:60 *V/V*).

Flow rate 0.7 mL/min.

Detection Spectrophotometer at 243 nm.

Injection 20 µL of the test solution and reference solutions (a), (b) and (c).

Run time 2.6 times the retention time of prednicarbate.

Identification of impurities Use the chromatogram supplied with *prednicarbate for system suitability A CRS* and the chromatogram obtained with reference solution (a) to identify the peaks due to impurities B, C, D, E and F; use the chromatogram supplied with *prednicarbate for peak identification CRS* and the chromatogram obtained with reference solution (b) to identify the peak due to impurity G.

Relative retention With reference to prednicarbate (retention time = about 20 min): impurity B = about 0.25; impurity C = about 0.35; impurity D = about 0.39; impurity E = about 0.6; impurity F = about 1.2; impurity G = about 2.4.

System suitability Reference solution (a):

— *resolution*: minimum 3.0 between the peaks due to prednicarbate and impurity F; minimum 1.5 between the peaks due to impurities C and D.

Calculation of percentage contents:

— for each impurity, use the concentration of prednicarbate in reference solution (c).

Limits:

— *impurity F*: maximum 0.8 per cent;

— *impurity C*: maximum 0.5 per cent;

— *impurity E*: maximum 0.3 per cent;

— *impurities B, D*: for each impurity, maximum 0.2 per cent;

— *impurity G*: maximum 0.15 per cent;

— *unspecified impurities*: for each impurity, maximum 0.10 per cent;

— *total*: maximum 2.0 per cent;

— *reporting threshold*: 0.05 per cent.

Loss on drying (*2.2.32*)

Maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C.

ASSAY

Liquid chromatography (*2.2.29*) as described in the test for related substances with the following modification.

Injection Test solution and reference solution (d).

Calculate the percentage content of $C_{27}H_{36}O_8$ taking into account the assigned content of *prednicarbate CRS*.

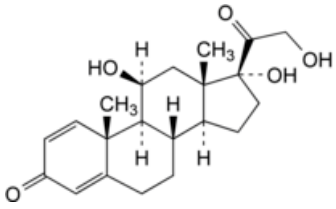
STORAGE

Protected from light.

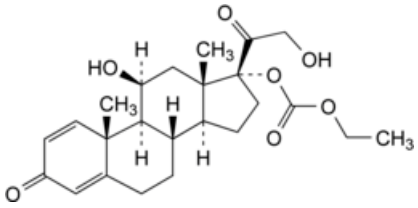
IMPURITIES

Specified impurities *B, C, D, E, F, G.*

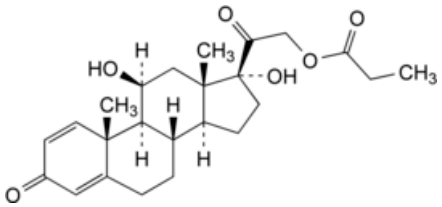
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical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



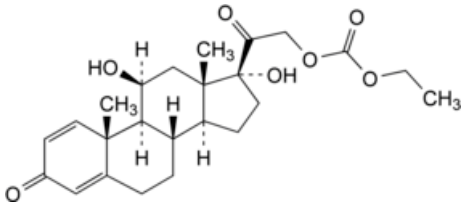
A. 11β,17,21-trihydroxypregna-1,4-diene-3,20-dione (prednisolone),



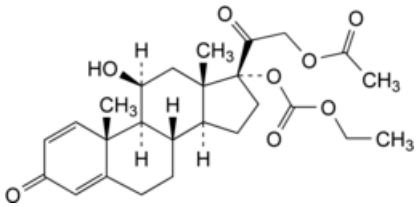
B. ethyl 11β,21-dihydroxy-3,20-dioxopregna-1,4-dien-17-yl carbonate (prednisolone 17-ethylcarbonate),



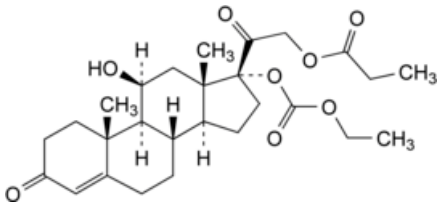
C. 11β,17-dihydroxy-3,20-dioxopregna-1,4-dien-21-yl propanoate (prednisolone 21-propanoate),



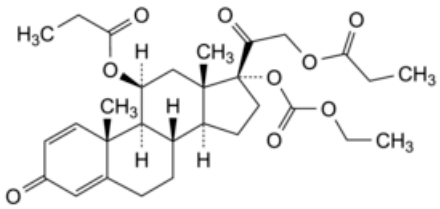
D. ethyl 11β,17-dihydroxy-3,20-dioxopregna-1,4-dien-21-yl carbonate (prednisolone 21-ethylcarbonate),



E. 11β-hydroxy-3,20-dioxopregna-1,4-diene-17,21-diyl 21-acetate 17-(ethyl carbonate) (prednisolone 21-acetate 17-ethylcarbonate),



F. 11β-hydroxy-3,20-dioxopregn-4-ene-17,21-diyl 17-(ethyl carbonate) 21-propanoate (1,2-dihydroprednicarbate),



G. 3,20-dioxo-11β-pregna-1,4-diene-11,17,21-triyl 17-(ethyl carbonate) 11,21-dipropanoate (prednicarbate 11-propanoate).

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