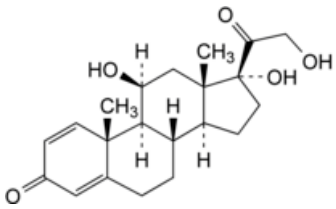
Edition: BP 2025 (Ph. Eur. 11.6 update)

Prednisolone

General Notices

(Ph. Eur. monograph 0353)



$C_{21}H_{28}O_5$ 360.5 *50-24-8*

Action and use

Glucocorticoid.

Preparations

Prednisolone Tablets

Prednisolone Gastro-resistant Tablets

Ph Eur

DEFINITION

11β,17,21-Trihydroxypregna-1,4-diene-3,20-dione.

Content

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

CHARACTERS

Appearance

White or almost white, crystalline, hygroscopic powder.

Solubility

Very slightly soluble in water, soluble in ethanol (96 per cent) and in methanol, sparingly soluble in acetone, slightly soluble in methylene chloride.

It shows polymorphism (*5.9*).

IDENTIFICATION

First identification: A, B.

Second identification: C, D.

A. Infrared absorption spectrophotometry (2.2.24).

Comparison prednisolone 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 acetone R, evaporate to dryness on a water-bath and record new spectra using the residues.

B. Examine the chromatograms obtained in the assay.

Results The principal peak in the chromatogram obtained with test solution (b) is similar in retention time and size to the principal peak in the chromatogram obtained with reference solution (d).

C. 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 prednisolone 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.

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.

D. Add about 2 mg to 2 mL of sulfuric acid R and shake to dissolve. Within 5 min, an intense red colour develops. When examined in ultraviolet light at 365 nm, a brownish-red fluorescence is seen. Add this solution to 10 mL of water R and mix. The colour fades and there is a strong yellowish-green fluorescence in ultraviolet light at 365 nm.

TESTS

Specific optical rotation (2.2.7)

+ 113 to + 119 (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). *Carry out the test protected from light.*

Solvent mixture acetonitrile R, water R (40:60 *V/V*).

Test solution (a) Dissolve 10 mg of the substance to be examined in the solvent mixture and dilute to 20.0 mL with the solvent mixture.

Test solution (b) Dissolve 25.0 mg of the substance to be examined in the solvent mixture and dilute to 20.0 mL with the solvent mixture. Dilute 1.0 mL of the solution to 10.0 mL with the solvent mixture.

Reference solution (a) Dissolve 5 mg of *prednisolone for system suitability CRS* (containing impurities A, B and C) in the solvent mixture and dilute to 10 mL with the solvent mixture.

Reference solution (b) Dissolve 5 mg of *prednisolone for peak identification CRS* (containing impurities F and J) in the solvent mixture and dilute to 10 mL with the solvent mixture.

Reference solution (c) Dilute 1.0 mL of test solution (a) to 100.0 mL with the solvent mixture. Dilute 1.0 mL of this solution to 10.0 mL with the solvent mixture.

Reference solution (d) Dissolve 25.0 mg of *prednisolone CRS* in the solvent mixture and dilute to 20.0 mL with the solvent mixture. Dilute 1.0 mL of the solution to 10.0 mL with the solvent mixture.

Column:

— *size*: *l* = 0.15 m, Ø = 4.6 mm;

— *stationary phase*: *end-capped octadecylsilyl silica gel for chromatography compatible with 100 per cent aqueous mobile phases R* (3 µm);

— *temperature*: 40 °C.

Mobile phase:

— *mobile phase A*: *water for chromatography R*;

— *mobile phase B*: *acetonitrile R*, *methanol R* (50:50 *V/V*);

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 14	60	40
14 - 20	60 → 20	40 → 80
20 - 25	20	80

Flow rate 1 mL/min.

Detection Spectrophotometer at 254 nm.

Injection 10 µL of test solution (a) and reference solutions (a), (b) and (c).

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

Relative retention With reference to prednisolone (retention time = about 12 min): impurity F = about 0.7; impurity B = about 0.9; impurity A = about 1.05; impurity J = about 1.5; impurity C = about 1.7.

System suitability Reference solution (a):

— *peak-to-valley ratio*: minimum 3, where H_p = height above the baseline of the peak due to impurity A and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to prednisolone.

Limits:

— *impurity A*: not more than 10 times the area of the principal peak in the chromatogram obtained with reference solution (c) (1.0 per cent);

— *impurity F*: not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.5 per cent);

— *impurities B, C, J*: for each impurity, not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.3 per cent);

— *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (c) (0.10 per cent);

— *total*: not more than 15 times the area of the principal peak in the chromatogram obtained with reference solution (c) (1.5 per cent);

— *disregard limit*: 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.05 per cent).

Loss on drying (*2.2.32*)

Maximum 1.0 per cent, determined on 0.500 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 (b) and reference solution (d).

Calculate the percentage content of $C_{21}H_{28}O_5$ taking into account the assigned content of *prednisolone CRS*.

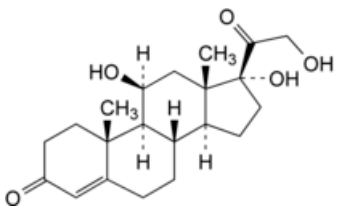
STORAGE

In an airtight container, protected from light.

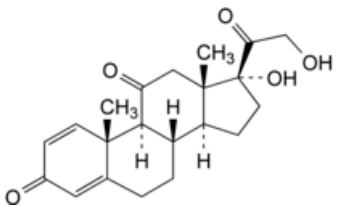
IMPURITIES

Specified impurities *A, B, C, F, J.*

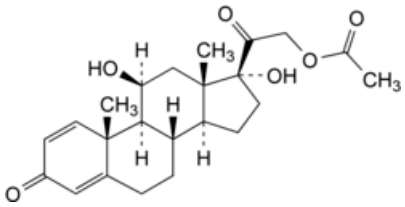
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical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



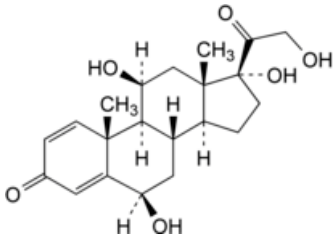
A. 11β,17,21-trihydroxypregn-4-ene-3,20-dione (hydrocortisone),



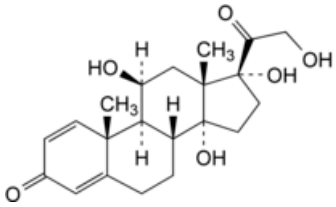
B. 17,21-dihydroxypregna-1,4-diene-3,11,20-trione (prednisone),



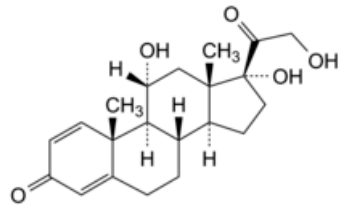
C. 11β,17-dihydroxy-3,20-dioxopregna-1,4-dien-21-yl acetate (prednisolone acetate),



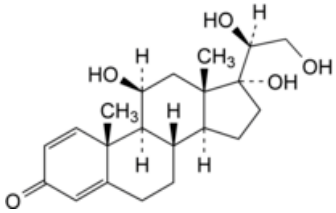
D. 6β,11β,17,21-tetrahydroxypregna-1,4-diene-3,20-dione (6β-hydroxyprednisolone),



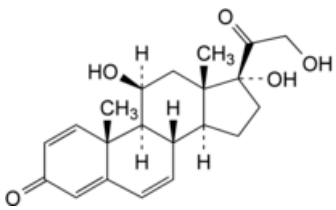
E. 11β,14α,17,21-tetrahydroxypregna-1,4-diene-3,20-dione (14α-hydroxyprednisolone),



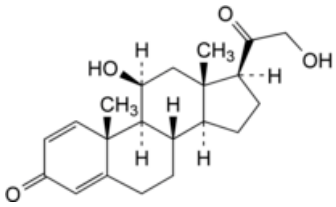
F. 11α,17,21-trihydroxypregna-1,4-diene-3,20-dione (11-*epi*-prednisolone),



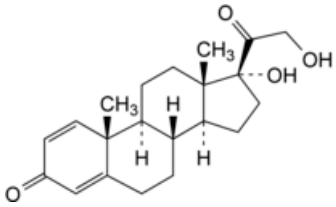
G. 11β,17,20*S*,21-tetrahydroxypregna-1,4-dien-3-one ((20*S*)-hydroxyprednisolone),



H. 11β,17,21-trihydroxypregna-1,4,6-triene-3,20-dione (Δ^6-prednisolone),



I. 11β,21-dihydroxypregna-1,4-diene-3,20-dione (17-deoxyprednisolone),



J. 17,21-dihydroxypregna-1,4-diene-3,20-dione (11-deoxyprednisolone).

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