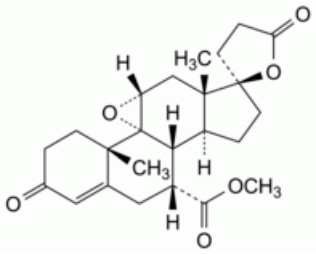
Edition: BP 2025 (Ph. Eur. 11.6 update)

Eplerenone

General Notices

(Ph. Eur. monograph 2765)



$C_{24}H_{30}O_6$ 414.5 *107724-20-9*

Action and use

Aldosterone receptor antagonist; antihypertensive.

Preparation

Eplerenone Tablets

Ph Eur

DEFINITION

9,11α-Epoxy-7α-(methoxycarbonyl)-3-oxo-17α-pregn-4-ene-21,17-carbolactone.

Content

97.5 per cent to 102.0 per cent (anhydrous substance).

CHARACTERS

Appearance

White, almost white or slightly yellow, crystalline powder.

Solubility

Slightly soluble in water, freely soluble in methylene chloride, slightly soluble in ethanol (96 per cent).

It shows polymorphism (*5.9*).

IDENTIFICATION

Infrared absorption spectrophotometry (2.2.24).

Comparison *eplerenone CRS*.

If the spectra obtained in the solid state show differences, dissolve the substance to be examined and the reference substance separately in *methanol R*, evaporate to dryness and record new spectra using the residues.

TESTS

Specific optical rotation (2.2.7)

-16.0 to -14.0.

Dissolve 0.250 g in *acetonitrile R* and dilute to 25.0 mL with the same solvent.

Related substances

Liquid chromatography (2.2.29).

Solvent mixture *acetonitrile R*, *methanol R*, *water R* (25:25:50 *V/V/V*).

Test solution (a) Dissolve 25.0 mg of the substance to be examined in the solvent mixture and dilute to 50.0 mL with the solvent mixture.

Test solution (b) Dilute 1.0 mL of test solution (a) to 10.0 mL with the solvent mixture.

Reference solution (a) Dissolve 5 mg of *eplerenone for system suitability CRS* (containing impurities A and D) in the solvent mixture and dilute to 10.0 mL with the solvent mixture.

Reference solution (b) Dissolve 5 mg of *eplerenone for peak identification CRS* (containing impurity B) in the solvent mixture and dilute to 10.0 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 *eplerenone CRS* in the solvent mixture and dilute to 50.0 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*: *base-deactivated end-capped octadecylsilyl silica gel for chromatography R* (3 µm);

— *temperature*: 30 °C.

Mobile phase:

— *mobile phase A*: 0.1 per cent *V/V* solution of *phosphoric acid R*;

— *mobile phase B*: *phosphoric acid R*, *acetonitrile R*, *methanol R* (0.1:40:60 *V/V/V*);

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 25	54	46
25 - 32	54 → 40	46 → 60
32 - 45	40	60

Flow rate 1.0 mL/min.

Detection Spectrophotometer at 240 nm.

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

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

Relative retention With reference to eplerenone (retention time = about 9 min): impurity D = about 0.71; impurity A = about 0.74; impurity B = about 1.2.

System suitability Reference solution (a):

— *peak-to-valley ratio*: minimum 5.0, where H_p = height above the baseline of the peak due to impurity D and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to impurity A.

Calculation of percentage contents:

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

Limits:

— *impurities A, B*: for each impurity, maximum 0.3 per cent;

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

— *total*: maximum 0.6 per cent;

— *reporting threshold*: 0.05 per cent.

Water (*2.5.12*)

Maximum 0.5 per cent, determined on 1.000 g.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

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

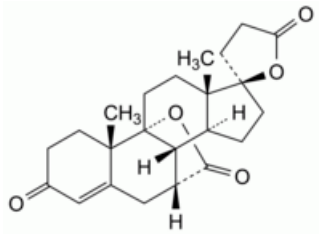
Injection Test solution (b) and reference solution (d).

Calculate the percentage content of $C_{24}H_{30}O_6$ taking into account the assigned content of *eplerenone CRS*.

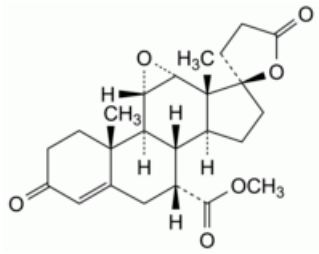
IMPURITIES

Specified impurities *A, B.*

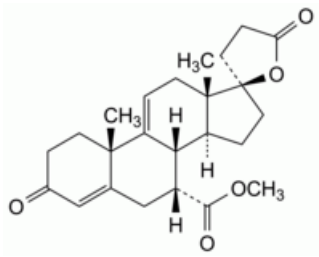
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical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



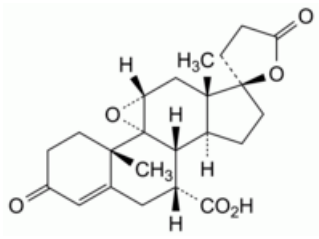
A. 3-oxo-17α-pregn-4-ene-7α,9:21,17-dicarbolactone,



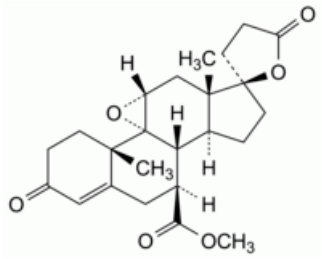
B. 11α,12α-epoxy-7α-(methoxycarbonyl)-3-oxo-17α-pregn-4-ene-21,17-carbolactone,



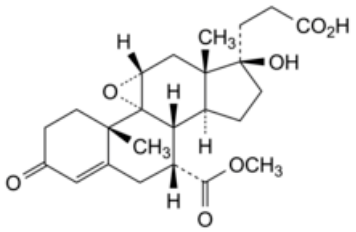
C. 7α-(methoxycarbonyl)-3-oxo-17α-pregna-4,9(11)-diene-21,17-carbolactone,



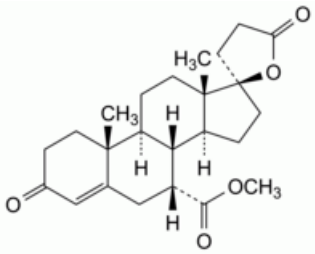
D. (2′*R*)-9,11α-epoxy-3,5′-dioxo-4′,5′-dihydro-3′*H*-spiro[androst-4-ene-17,2′-furan]-7α-carboxylic acid,



E. 9,11α-epoxy-7β-(methoxycarbonyl)-3-oxo-17α-pregn-4-ene-21,17-carbolactone,



F. 9,11α-epoxy-17-hydroxy-7α-(methoxycarbonyl)-3-oxo-17α-pregn-4-ene-21-carboxylic acid,



G. 7α-(methoxycarbonyl)-3-oxo-17α-pregn-4-ene-21,17-carbolactone.

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