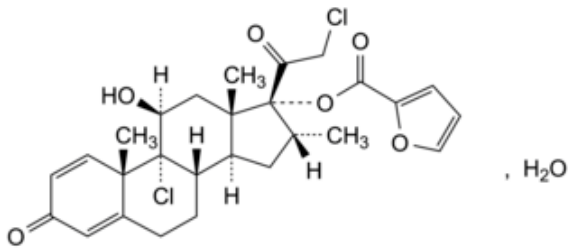
Edition: BP 2025 (Ph. Eur. 11.6 update)

Mometasone Furoate Monohydrate

General Notices

(Ph. Eur. monograph 2858)



$C_{27}H_{30}Cl_2O_6,H_2O$ 539.4 *141646-00-6*

Action and use

Glucocorticoid.

Ph Eur

DEFINITION

9,21-Dichloro-11β-hydroxy-16α-methyl-3,20-dioxopregna-1,4-dien-17-yl furan-2-carboxylate monohydrate.

Content

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

CHARACTERS

Appearance

White or almost white powder.

Solubility

Practically insoluble in water, soluble in acetone and in methylene chloride, slightly soluble in ethanol (96 per cent).

IDENTIFICATION

A. Infrared absorption spectrophotometry (*2.2.24*).

Comparison *mometasone furoate monohydrate CRS*.

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 (c).

C. Water (see Tests).

TESTS

Specific optical rotation (*2.2.7*)

+ 50 to + 55 (anhydrous substance).

Dissolve 50.0 mg in *ethanol (96 per cent) R* and dilute to 10.0 mL with the same solvent.

Related substances

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

Solvent mixture Mix 200 mL of *acetonitrile R* and 200 mL of *water R*, then add 0.4 mL of *acetic acid R*.

Test solution (a) Dissolve 25.0 mg of the substance to be examined in 15 mL of *acetonitrile R* and dilute to 50.0 mL with the solvent mixture.

Test solution (b) Dilute 5.0 mL of test solution (a) to 25.0 mL with the solvent mixture.

Reference solution (a) Dissolve 5 mg of *mometasone furoate for system suitability CRS* (containing impurity C) in 3 mL of *acetonitrile R* and dilute to 10.0 mL with the solvent mixture.

Reference solution (b) 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 (c) Dissolve 25.0 mg of *mometasone furoate monohydrate CRS* in 15 mL of *acetonitrile R* and dilute to 50.0 mL with the solvent mixture. Dilute 5.0 mL of the solution to 25.0 mL with the solvent mixture.

Column:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

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

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

Flow rate 1.0 mL/min.

Detection Spectrophotometer at 254 nm.

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

Run time 3.5 times the retention time of mometasone furoate.

Identification of impurities Use the chromatogram supplied with *mometasone furoate for system suitability CRS* and the chromatogram obtained with reference solution (a) to identify the peak due to impurity C.

Relative retention With reference to mometasone furoate (retention time = about 24 min): impurity C = about 0.9.

System suitability Reference solution (a):

— *resolution*: minimum 2.5 between the peaks due to impurity C and mometasone furoate.

Limits:

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

— *total*: not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.3 per cent);

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

Water (*2.5.12*)

2.5 per cent to 4.0 per cent, determined on 0.200 g.

ASSAY

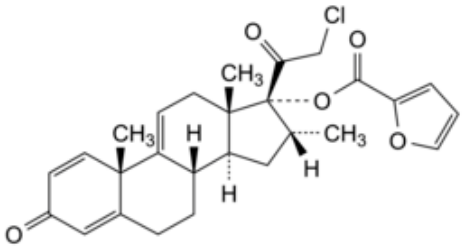
Liquid chromatography (*2.2.29*) as described in the test for related substances with the following modification.

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

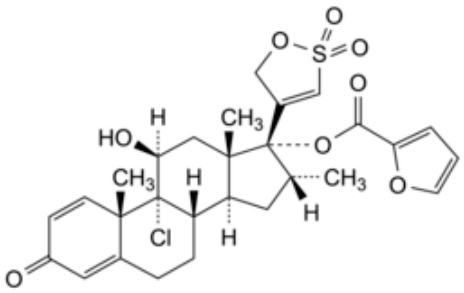
Calculate the percentage content of $C_{27}H_{30}Cl_2O_6$ taking into account the assigned content of *mometasone furoate monohydrate CRS*.

IMPURITIES

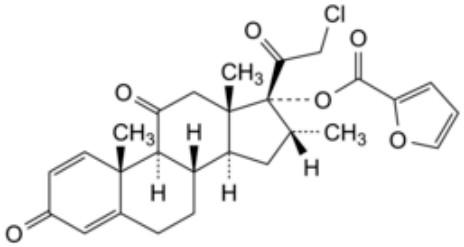
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical 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, B, C, D, E, F, G, H, I, J, K, L, M, N, O, P, Q, R, S, T, U.



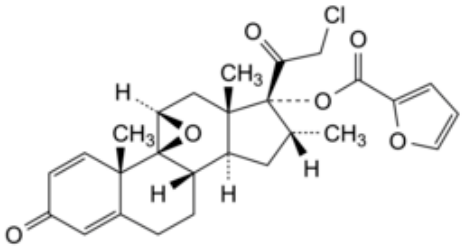
A. 21-chloro-16α-methyl-3,20-dioxopregna-1,4,9(11)-trien-17-yl furan-2-carboxylate,



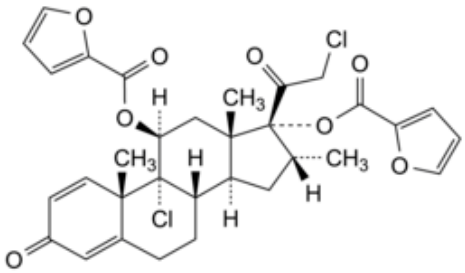
B. 9-chloro-17β-(2,2-dioxo-2,5-dihydro-1,2λ^{6}-oxathiol-4-yl)-11β-hydroxy-16α-methyl-3-oxoandrosta-1,4-dien-17α-yl furan-2-carboxylate,



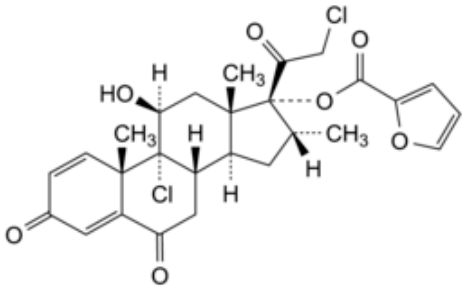
C. 21-chloro-16α-methyl-3,11,20-trioxopregna-1,4-dien-17-yl furan-2-carboxylate,



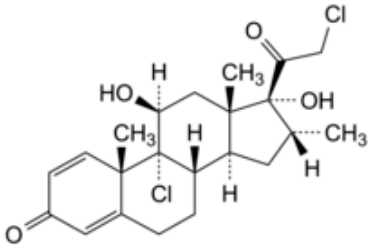
D. 21-chloro-9,11β-epoxy-16α-methyl-3,20-dioxo-9β-pregna-1,4-dien-17-yl furan-2-carboxylate,



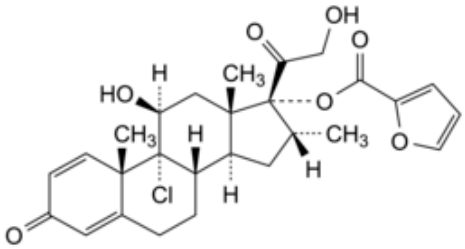
E. 9,21-dichloro-16α-methyl-3,20-dioxopregna-1,4-diene-11β,17-diyl di(furan-2-carboxylate),



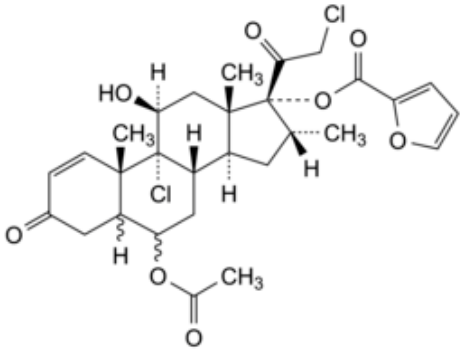
F. 9,21-dichloro-11β-hydroxy-16α-methyl-3,6,20-trioxopregna-1,4-dien-17-yl furan-2-carboxylate,



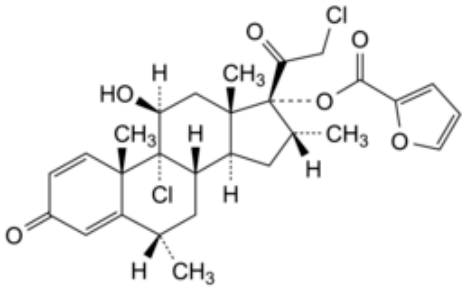
G. 9,21-dichloro-11β,17-dihydroxy-16α-methylpregna-1,4-diene-3,20-dione (mometasone),



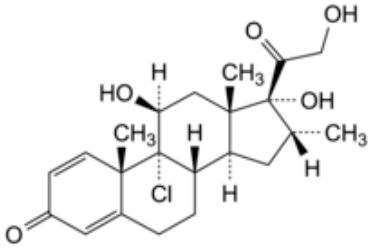
H. 9-chloro-11β,21-dihydroxy-16α-methyl-3,20-dioxopregna-1,4-dien-17-yl furan-2-carboxylate,



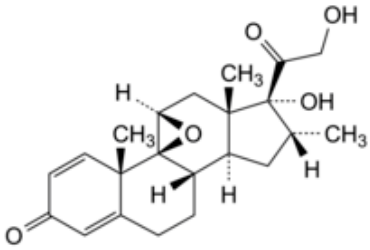
I. 6ξ-acetoxy-9,21-dichloro-11β-hydroxy-16α-methyl-3,20-dioxo-5ξ-pregn-1-en-17-yl furan-2-carboxylate,



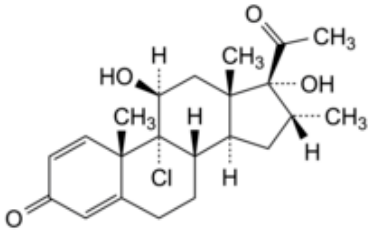
J. 9,21-dichloro-11β-hydroxy-6α,16α-dimethyl-3,20-dioxopregna-1,4-dien-17-yl furan-2-carboxylate,



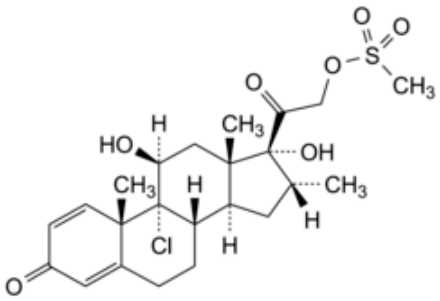
K. 9-chloro-11β,17,21-trihydroxy-16α-methylpregna-1,4-diene-3,20-dione,



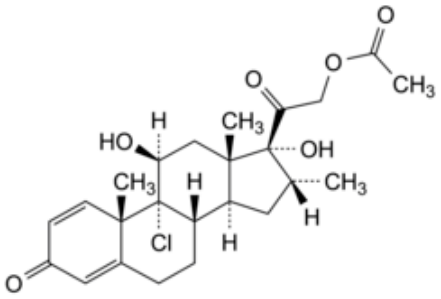
L. 9,11β-epoxy-17,21-dihydroxy-16α-methyl-9β-pregna-1,4-diene-3,20-dione,



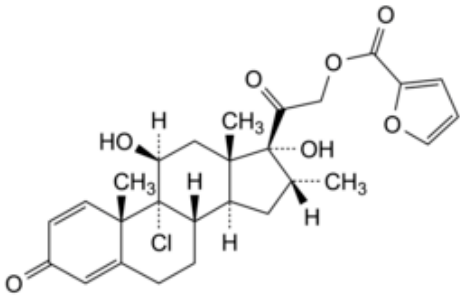
M. 9-chloro-11β,17-dihydroxy-16α-methylpregna-1,4-diene-3,20-dione,



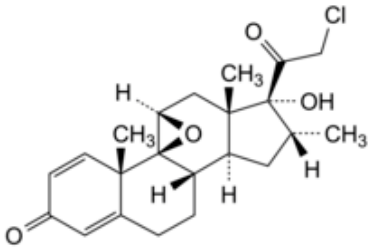
N. 9-chloro-11β,17-dihydroxy-16α-methyl-3,20-dioxopregna-1,4-dien-21-yl methanesulfonate,



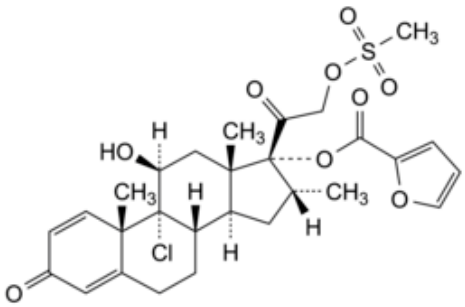
O. 9-chloro-11β,17-dihydroxy-16α-methyl-3,20-dioxopregna-1,4-dien-21-yl acetate,



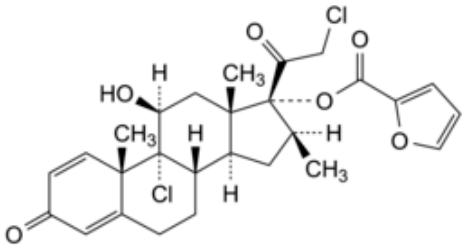
P. 9-chloro-11β,17-dihydroxy-16α-methyl-3,20-dioxopregna-1,4-dien-21-yl furan-2-carboxylate,



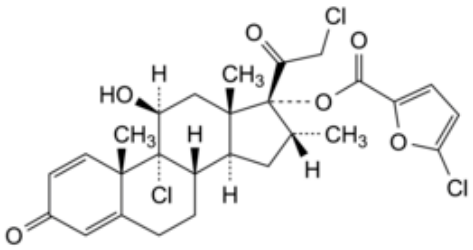
Q. 21-chloro-9,11β-epoxy-17-hydroxy-16α-methyl-9β-pregna-1,4-diene-3,20-dione,



R. 9-chloro-11β-hydroxy-16α-methyl-21-[(methylsulfonyl)oxy]-3,20-dioxopregna-1,4-dien-17-yl furan-2-carboxylate,



S. 9,21-dichloro-11β-hydroxy-16β-methyl-3,20-dioxopregna-1,4-dien-17-yl furan-2-carboxylate,



T. 9,21-dichloro-11β-hydroxy-16α-methyl-3,20-dioxopregna-1,4-dien-17-yl 5-chlorofuran-2-carboxylate,

U. unknown structure.

Ph Eur