Reference solution. Mix 6 mL of lead standard solution (1 ppm Pb) (obtained by diluting *lead standard solution (100 ppm Pb) R* with *ethanol (96 per cent) R*) with 2 mL of the prescribed solution and 4 mL of *water R*.

Blank solution. Mix 10 mL of *ethanol (96 per cent) R* and 2 mL of the prescribed solution.

To each solution, add 2 mL of *buffer solution pH 3.5 R*. Mix and add to 1.2 mL of *thioacetamide reagent R*. Mix immediately. Filter the solutions through a membrane filter (nominal pore size 0.45 µm) (*2.4.8*). Carry out the filtration slowly and uniformly, applying moderate and constant pressure to the piston. Compare the spots on the filters obtained with the different solutions. The test is invalid if the reference solution does not show a slight brown colour compared to the blank solution. The substance to be examined complies with the test if the brown colour of the spot resulting from the test solution is not more intense than that of the spot resulting from the reference solution.

Loss on drying (*2.2.32*): maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C.

Sulfated ash (*2.4.14*): maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.200 g in a mixture of 5 mL of *acetic anhydride R* and 50 mL of *anhydrous 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 24.22 mg of $C_9H_{14}N_4O_4$.

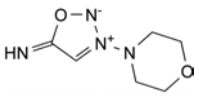
STORAGE

Protected from light.

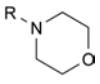
IMPURITIES

Specified impurities: B, E.

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, C, D.*



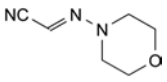
A. 3-(morpholin-4-yl)sydnonimine (linsidomine),



B. R = NO: 4-nitrosomorpholine,

D. R = CHO: morpholine-4-carbaldehyde,

E. R = H: morpholine,

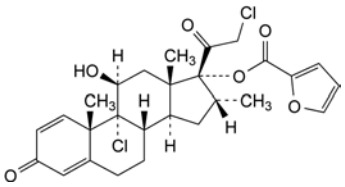


C. (2*E*)-(morpholin-4-ylimino)acetonitrile.

01/2008:1449
corrected 6.0

MOMETASONE FUROATE

Mometasoni furoas



$C_{27}H_{30}Cl_2O_6$ M_r 521.4
[83919-23-7]

DEFINITION

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

Content: 97.0 per cent to 103.0 per cent (dried 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).

mp: about 220 °C, with decomposition.

IDENTIFICATION

First identification: A, B.

Second identification: B, C, D.

A. Infrared absorption spectrophotometry (*2.2.24*).

Preparation: discs.

Comparison: *mometasone furoate CRS*.

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

Test solution. Dissolve 10 mg of the substance to be examined in *methylene chloride R* and dilute to 10 mL with the same solvent.

Reference solution (a). Dissolve 20 mg of *mometasone furoate CRS* in *methylene chloride R* and dilute to 20 mL with the same solvent.

Reference solution (b). Dissolve 10 mg of *anhydrous beclometasone dipropionate CRS* in reference solution (a) and dilute to 10 mL with reference solution (a).

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

Mobile phase: add a mixture of 1.2 volumes of *water R* and 8 volumes of *methanol R* to a mixture of 15 volumes of *ether R* and 77 volumes of *methylene chloride R*.

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 sulfuric 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, when examined in ultraviolet light at 365 nm, may not be completely separated.

Monographs M

C. Add about 2 mg to 2 mL of *sulfuric acid R* and shake to dissolve. Within 15 min a light yellow colour develops. When examined in ultraviolet light at 365 nm, no fluorescence is seen. Add this solution to 10 mL of *water R* and mix. The colour fades and there is no fluorescence.

D. Mix 80 mg with 0.30 g of *anhydrous sodium carbonate R* and ignite in a crucible until an almost white residue is obtained. Allow to cool and dissolve the residue in 5 mL of *dilute nitric acid R*; filter. To 1 mL of the filtrate add 1 mL of *water R*. The solution gives reaction (a) of chlorides (*2.3.1*).

TESTS

Specific optical rotation (*2.2.7*): + 50 to + 55 (dried 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 50 mL of *acetonitrile R* and 50 mL of *water R*, then add 0.1 mL of *acetic acid R*.

Test solution. Dissolve 20.0 mg of the substance to be examined in 4.0 mL of *acetonitrile R* and dilute to 20.0 mL with the solvent mixture.

Reference solution (a). Dissolve 2 mg of *mometasone furoate CRS* and 6 mg of *anhydrous beclometasone dipropionate CRS* in the solvent mixture, then dilute to 10.0 mL with the solvent mixture. Dilute 0.25 mL of this solution to 10.0 mL with the solvent mixture.

Reference solution (b). Dilute 1.0 mL of the test solution to 20.0 mL with the solvent mixture. Dilute 1.0 mL of this solution to 10.0 mL with the solvent mixture.

Column:

– *size*: *l* = 0.25 m, Ø = 4.6 mm;

– *stationary phase*: *octadecylsilyl silica gel for chromatography R* (5 µm).

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

Flow rate: 1 mL/min.

Detection: spectrophotometer at 254 nm.

Injection: 20 µL.

Run time: twice the retention time of mometasone furoate.

Retention time: mometasone furoate = about 17 min; beclometasone dipropionate = about 22 min.

System suitability: reference solution (a):

– *resolution*: minimum 6 between the peaks due to mometasone furoate and beclometasone dipropionate; if necessary, adjust the concentration of acetonitrile in the mobile phase.

Limits:

– *impurities A, B, C, D, E, F, G, H, I*: for each impurity, not more than 0.6 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.3 per cent);

– *total*: not more than 1.2 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.6 per cent);

– *disregard limit*: 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (b) (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.

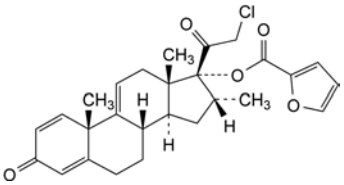
ASSAY

Dissolve 50.0 mg in *ethanol (96 per cent) R* and dilute to 100.0 mL with the same solvent. Dilute 2.0 mL of this solution to 100.0 mL with *ethanol (96 per cent) R*. Measure the absorbance (*2.2.25*) at the absorption maximum at 249 nm.

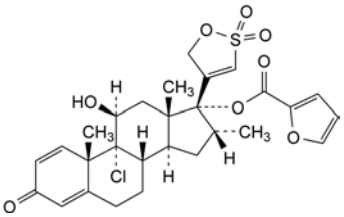
Calculate the content of $C_{27}H_{30}Cl_2O_6$ taking the specific absorbance to be 481.

IMPURITIES

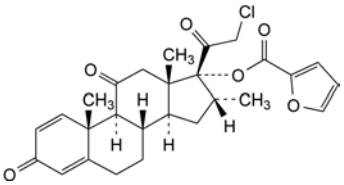
Specified impurities: *A, B, C, D, E, F, G, H, I.*



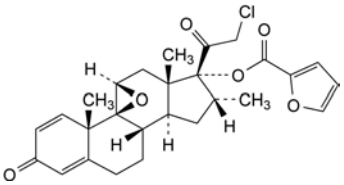
A. 21-chloro-16α-methyl-3,20-dioxopregna-1,4,9(11)-trien-17-yl furan-2-carboxylate,



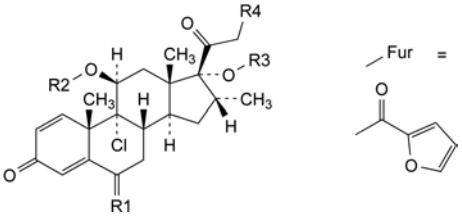
B. 4-[9-chloro-17-[(furan-2-ylcarbonyl)oxy]-11β-hydroxy-16α-methyl-3-oxoandrosta-1,4-dien-17β-yl]-5*H*-1,2-oxathiole 2,2-dioxide,



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,

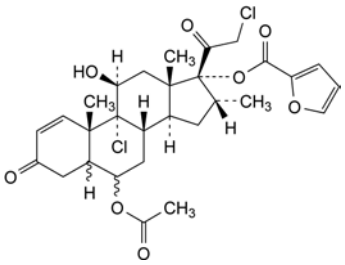


E. R1 = H_2, R2 = R3 = Fur, R4 = Cl: 9,21-dichloro-16α-methyl-3,20-dioxopregna-1,4-diene-11β,17-diyl bis(furan-2-carboxylate),

F. R1 = O, R2 = H, R3 = Fur, R4 = Cl: 9,21-dichloro-11β-hydroxy-16α-methyl-3,6,20-trioxopregna-1,4-dien-17-yl furan-2-carboxylate,

G. R1 = H_2, R2 = R3 = H, R4 = Cl: 9,21-dichloro-11β,17-dihydroxy-16α-methylpregna-1,4-diene-3,20-dione (mometasone),

H. R1 = H_2, R2 = H, R3 = Fur, R4 = OH: 9-chloro-11β,21-dihydroxy-16α-methyl-3,20-dioxopregna-1,4-dien-17-yl furan-2-carboxylate,

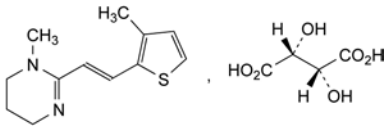


I. 9,21-dichloro-11β-hydroxy-16α-methyl-3,20-dioxo-5ξ-pregn-1-ene-6ξ,17-diyl 6-acetate 17-(furan-2-carboxylate).

01/2008:1546
corrected 6.0

MORANTEL HYDROGEN TARTRATE FOR VETERINARY USE

Moranteli hydrogenotartras ad usum veterinarium



$C_{16}H_{22}N_2O_6S$ M_r 370.4
[26155-31-7]

DEFINITION

1-Methyl-2-[(*E*)-2-(3-methylthiophen-2-yl)ethenyl]-1,4,5,6-tetrahydropyrimidine hydrogen tartrate.

Content: 98.5 per cent to 101.5 per cent (dried substance).

CHARACTERS

Appearance: white or pale yellow, crystalline powder.

Solubility: very soluble in water and in ethanol (96 per cent), practically insoluble in ethyl acetate.

IDENTIFICATION

First identification: B.

Second identification: A, C, D.

A. Melting point (*2.2.14*): 167 °C to 172 °C.

B. Infrared absorption spectrophotometry (*2.2.24*).
Comparison: *morantel hydrogen tartrate CRS.*

C. Dissolve about 10 mg in 1 mL of a 5 g/L solution of *ammonium vanadate R*. Evaporate to dryness. Add 0.1 mL of *sulfuric acid R*. A purple colour is produced.

D. Dissolve about 10 mg in 1 mL of *0.1 M sodium hydroxide*. Transfer to a separating funnel and shake with 5 mL of *methylene chloride R*. Discard the organic layer. Neutralise the aqueous layer with a few drops of *dilute hydrochloric acid R*. The solution gives reaction (b) of tartrates (*2.3.1*).

TESTS

Solution S. Dissolve 0.25 g in *carbon dioxide-free water R* and dilute to 25.0 mL with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution GY_6 or Y_6 (*2.2.2, Method II*).

pH (*2.2.3*): 3.3 to 3.9 for solution S.

Related substances. Liquid chromatography (*2.2.29*). *Carry out the test protected from light.*

Test solution. Dissolve 50.0 mg of the substance to be examined in the mobile phase and dilute to 100.0 mL with the mobile phase.

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

Reference solution (b). Dilute 2.0 mL of reference solution (a) to 100.0 mL with the mobile phase.

Reference solution (c). Expose 10 mL of reference solution (a) to daylight for 15 min before injection.

Reference solution (d). Dissolve 15.0 mg of *tartaric acid R* in the mobile phase and dilute to 100.0 mL with the mobile phase.

Column:
- *size*: *l* = 0.25 m, Ø = 4.6 mm;
- *stationary phase*: *base-deactivated end-capped octadecylsilyl silica gel for chromatography R* (5 μm).

Mobile phase: to a mixture of 0.35 volumes of *triethylamine R* and 85 volumes of *water R* adjusted to pH 2.5 with *phosphoric acid R*, add 5 volumes of *tetrahydrofuran R* and 10 volumes of *methanol R*.

Flow rate: 0.75 mL/min.

Detection: spectrophotometer at 226 nm.

Injection: 20 μL.

Run time: twice the retention time of morantel.

System suitability: reference solution (c):
- *resolution*: minimum of 2 between the principal peak and the preceding peak ((*Z*)-isomer).

Limits:
- *any impurity apart from the peak due to tartaric acid*: not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent);
- *total*: not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (1 per cent);
- *disregard limit*: the area of the principal peak in the chromatogram obtained with reference solution (b) (0.02 per cent).

Heavy metals (*2.4.8*): maximum 20 ppm.

1.0 g complies with test C. Prepare the reference solution using 2 mL of *lead standard solution (10 ppm Pb) R*.

Loss on drying (*2.2.32*): maximum 1.5 per cent, determined on 1.000 g by drying in an oven at 105 °C.

Sulfated ash (*2.4.14*): maximum 0.1 per cent, determined on 1.0 g.

ASSAY

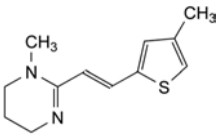
Dissolve 0.280 g in 40 mL of *anhydrous acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M perchloric acid* is equivalent to 37.04 mg of $C_{16}H_{22}N_2O_6S$.

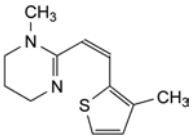
STORAGE

Protected from light.

IMPURITIES



A. 1-methyl-2-[(*E*)-2-(4-methylthiophen-2-yl)ethenyl]-1,4,5,6-tetrahydropyrimidine,



B. 1-methyl-2-[(*Z*)-2-(3-methylthiophen-2-yl)ethenyl]-1,4,5,6-tetrahydropyrimidine,

Monographs M