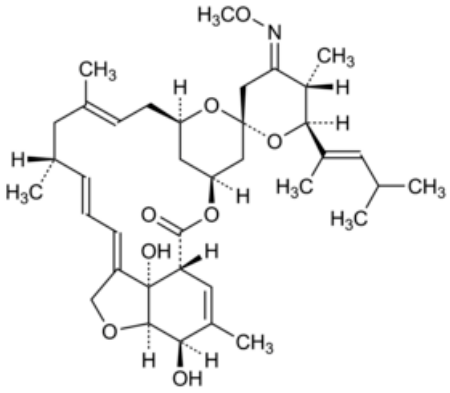
Edition: BP 2025 (Ph. Eur. 11.6 update)

Moxidectin

General Notices

(Moxidectin for Veterinary Use, Ph. Eur. monograph 1656)



$C_{37}H_{53}NO_8$ 640 *113507-06-5*

Action and use

Antihelminthic; ectoparasiticide.

Preparations

Moxidectin Injection

Moxidectin Oral Solution

Moxidectin Oromucosal Gel

Moxidectin Pour-on

Ph Eur

DEFINITION

(1^{3a}*S*,1^{4}*R*,1^{7}*R*,1^{7a}*R*,2′*R*,4′*E*,4^{2}*R*,4^{4}*S*,5′*S*,6*E*,6′*S*,9*R*,10*E*,12*E*)-1^{3a},1^{7}-Dihydroxy-4′-(methoxyimino)-1^{6},5′,7,9-tetramethyl-6′-[(2*E*)-4-methylpent-2-en-1-yl]-1^{3a},1^{4},1^{7},1^{7a}-tetrahydro-1^{2}*H*-3-oxa-1(4,3)-[1]benzofurana-4(4,2)-oxanaspiro[cyclododecaphane-6,10,12(1^{3})-trien-4^{6},2'-oxan]-2-one ((6*R*,23*E*,25*S*)-5-*O*-demethyl-28-deoxy-6,28-epoxy-23-(methoxyimino)-25-[(2*E*)-4-methylpent-2-en-1-yl]milbemycin B).

Semi-synthetic product derived from a fermentation product.

It may contain suitable stabilisers such as antioxidants.

Content

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

CHARACTERS

Appearance

White or pale yellow, amorphous powder.

Solubility

Practically insoluble in water, very soluble in ethanol (96 per cent), slightly soluble in hexane.

IDENTIFICATION

Infrared absorption spectrophotometry (2.2.24).

Comparison *moxidectin CRS*.

TESTS

Appearance of solution

The solution is clear (2.2.1) and not more intensely coloured than reference solution GY_5 (2.2.2, *Method II*).

Dissolve 0.40 g in *benzyl alcohol R* and dilute to 20 mL with the same solvent.

Related substances

Liquid chromatography (2.2.29).

A. *Test solution*. Dissolve 25.0 mg of the substance to be examined in *acetonitrile R* and dilute to 25.0 mL with the same solvent.

Reference solution (a) Dilute 1.0 mL of the test solution to 100.0 mL with *acetonitrile R*.

Reference solution (b) Dissolve 5 mg of *moxidectin for system suitability CRS* (containing impurities A, B, C, D, E, F, G, H, I, J and K) in 5 mL of *acetonitrile R*.

Reference solution (c) Dissolve 25.0 mg of *moxidectin CRS* in *acetonitrile R* and dilute to 25.0 mL with the same solvent.

Column:

— *size*: *l* = 0.15 m, Ø = 3.9 mm;

— *stationary phase: end-capped octadecylsilyl silica gel for chromatography R* (4 µm);

— *temperature*: 50 °C.

Mobile phase Dissolve 7.7 g of *ammonium acetate R* in 400 mL of *water for chromatography R*, adjust to pH 4.8 with *glacial acetic acid R* and add 600 mL of *acetonitrile for chromatography R*.

Flow rate 2.5 mL/min.

Detection Spectrophotometer at 242 nm.

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

Run time 2 times the retention time of moxidectin.

Identification of impurities Use the chromatogram supplied with *moxidectin for system suitability CRS* and the chromatogram obtained with reference solution (b) to identify the peaks due to impurities A, B, C, D, E + F and G.

Relative retention With reference to moxidectin (retention time = about 12 min): impurity A = about 0.5; impurity B = about 0.7; impurity C = about 0.75; impurity D = about 0.94; impurities E and F = about 1.3-1.5; impurity G = about 1.6.

System suitability Reference solution (b):

— *peak-to-valley ratio*: minimum 3.0, 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 moxidectin.

Limits:

— *impurity D*: not more than 2.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (2.5 per cent);

— *sum of impurities E and F*: not more than 1.7 times the area of the principal peak in the chromatogram obtained with reference solution (a) (1.7 per cent);

— *impurities A, C, G*: for each impurity, not more than 1.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (1.5 per cent);

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

— *any other impurity eluting before impurity G*: for each impurity, not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent);

— *disregard limit*: 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent); disregard the peak due to the stabiliser (identify this peak, where applicable, by injecting a suitable reference solution).

B. *Test solution*. Dissolve 75.0 mg of the substance to be examined in *acetonitrile R* and dilute to 25.0 mL with the same solvent.

Reference solution (a) Dilute 1.0 mL of the test solution to 100.0 mL with *acetonitrile R*.

Reference solution (b) Dissolve 5 mg of *moxidectin for system suitability CRS* (containing impurities A, B, C, D, E, F, G, H, I, J and K) in 5 mL of *acetonitrile R*.

Column:

— *size*: *l* = 0.15 m, Ø = 3.9 mm;

— *stationary phase*: *end-capped octadecylsilyl silica gel for chromatography R* (4 µm);

— *temperature*: 35 °C.

Mobile phase Dissolve 3.8 g of *ammonium acetate R* in 250 mL of *water for chromatography R*, adjust to pH 4.2 with *acetic acid R* and add 750 mL of *acetonitrile for chromatography R*.

Flow rate 2.0 mL/min.

Detection Spectrophotometer at 242 nm.

Injection 10 µL.

Run time 10 times the retention time of moxidectin.

Identification of impurities Use the chromatogram supplied with *moxidectin for system suitability CRS* and the chromatogram obtained with reference solution (b) to identify the peaks due to impurities H + I, J and K.

Relative retention With reference to moxidectin (retention time = about 4 min): impurity G = about 1.4; impurities H and I = about 2.0; impurity J = about 2.2; impurity K = about 3.4.

System suitability Reference solution (b):

— *resolution*: baseline separation between the peaks due to impurities H + I and J.

Limits:

— *sum of impurities H and I*: not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (1.0 per cent);

— *impurities J, K*: for each impurity, not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent);

— *any other impurity eluting after impurity G*: for each impurity, not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent);

— *disregard limit*: 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent); disregard the peak due to the stabiliser (identify this peak, where applicable, by injecting a suitable reference solution).

Total of all impurities Calculate the sum of the impurities eluting from the start of the run to impurity G in test A, and from impurities H + I to the end of the run in test B. The total of all impurities is not more than 7.0 per cent.

Water (*2.5.12*)

Maximum 1.3 per cent, determined on 0.500 g.

Sulfated ash (*2.4.14*)

Maximum 0.2 per cent, determined on 1.0 g.

ASSAY

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

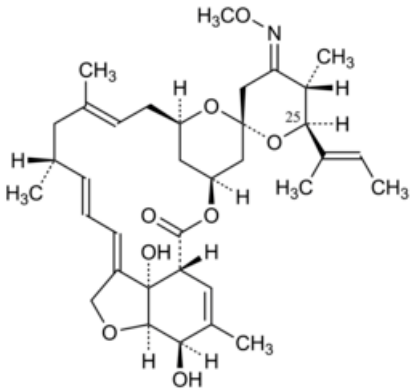
Injection Test solution and reference solution (c).

Calculate the percentage content of $C_{37}H_{53}NO_8$ taking into account the assigned content of *moxidectin CRS*.

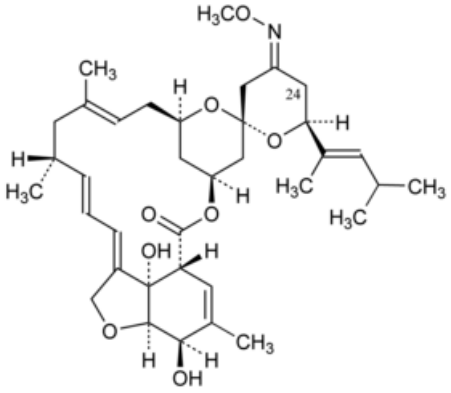
IMPURITIES

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

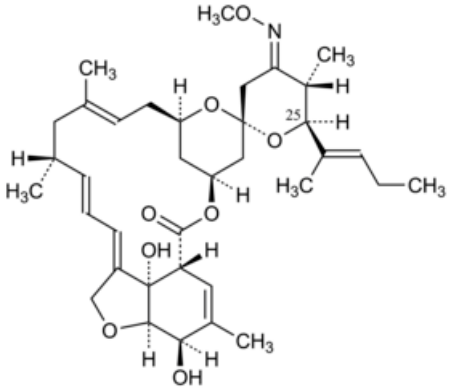
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical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



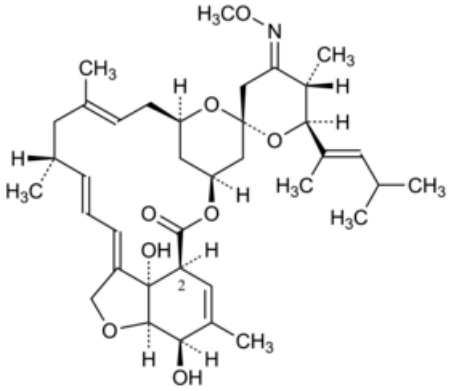
A. (6*R*,23*E*,25*S*)-25-[(2*E*)-but-2-en-2-yl]-5-*O*-demethyl-28-deoxy-6,28-epoxy-23-(methoxyimino)milbemycin B,



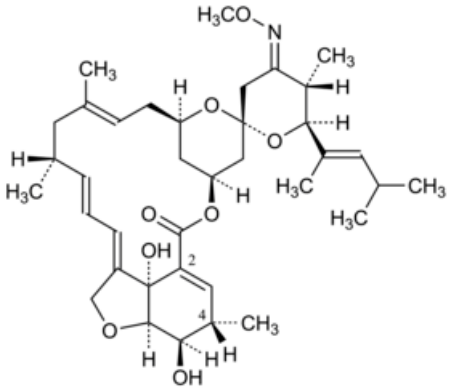
B. (6*R*,23*E*,25*S*)-5-*O*,24-didemethyl-28-deoxy-6,28-epoxy-23-(methoxyimino)-25-[(2*E*)-4-methylpent-2-en-1-yl]milbemycin B,



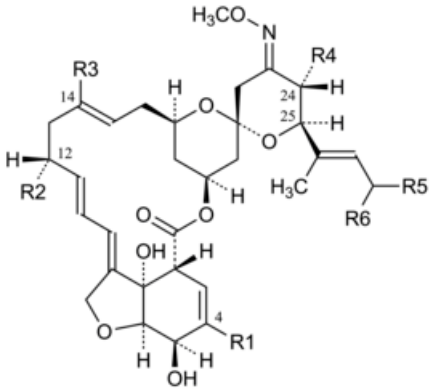
C. (6*R*,23*E*,25*S*)-5-*O*-demethyl-28-deoxy-6,28-epoxy-23-(methoxyimino)-25-[(2*E*)-pent-2-en-1-yl]milbemycin B,



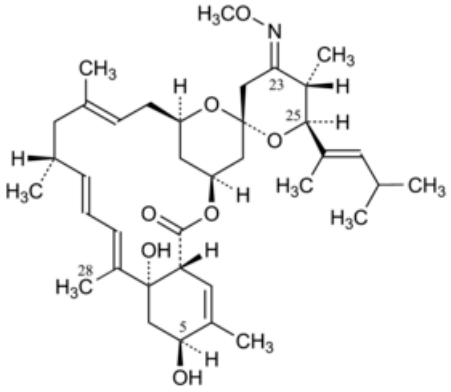
D. (6*R*,23*E*,25*S*)-5-*O*-demethyl-28-deoxy-6,28-epoxy-23-(methoxyimino)-25-[(2*E*)-4-methylpent-2-en-1-yl]-2-*epi*-milbemycin B,



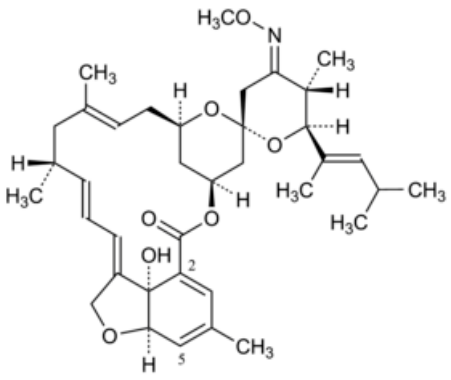
E. (1^{6}*S*,6*R*,23*E*,25*S*)-5-*O*-demethyl-28-deoxy-6,28-epoxy-23-(methoxyimino)-25-[(2*E*)-4-methylpent-2-en-1-yl]-1^{4}-dehydro-1^{6}-hydromilbemycin B,



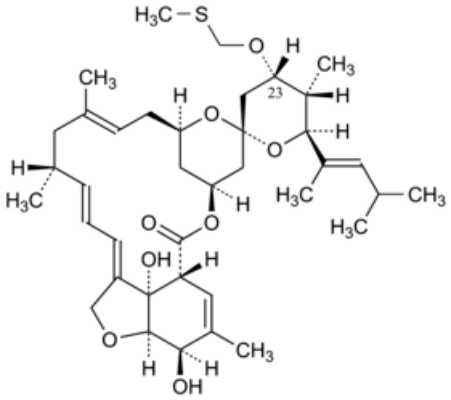
F. one of groups R1 to R6 is C_2H_5, the others are CH_3: *x*-demethyl-*x*-ethylmoxidectin,



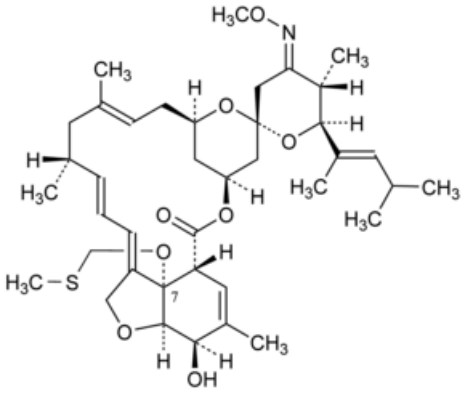
G. (23*E*,25*S*)-5-*O*-demethyl-28-deoxy-23-(methoxyimino)-25-[(2*E*)-4-methylpent-2-en-1-yl]milbemycin B,



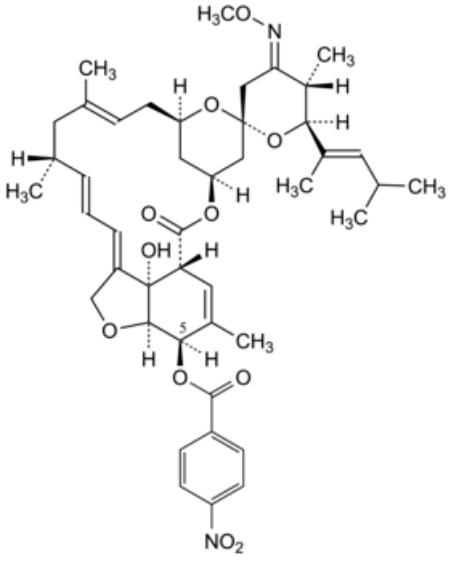
H. (6*R*,23*E*,25*S*)-5-demethoxy-28-deoxy-6,28-epoxy-23-(methoxyimino)-25-[(2*E*)-4-methylpent-2-en-1-yl]-2,5-didehydromilbemycin B,



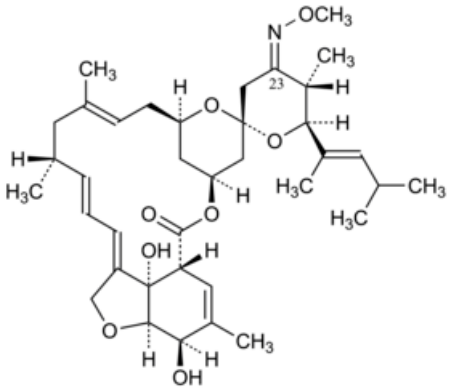
I. (6*R*,23*E*,25*S*)-5-*O*-demethyl-28-deoxy-6,28-epoxy-25-[(2*E*)-4-methylpent-2-en-1-yl]-23-[(methylsulfanyl)methoxy]milbemycin B,



J. (6*R*,23*E*,25*S*)-5-*O*-demethyl-28-deoxy-6,28-epoxy-23-(methoxyimino)-25-[(2*E*)-4-methylpent-2-en-1-yl]-7-*O*-[(methylsulfanyl)methyl]milbemycin B,



K. (6*R*,23*E*,25*S*)-5-*O*-demethyl-28-deoxy-6,28-epoxy-23-(methoxyimino)-25-[(2*E*)-4-methylpent-2-en-1-yl]-5-*O*-(4-nitrobenzoyl)milbemycin B,



L. (6*R*,23*Z*,25*S*)-5-*O*-demethyl-28-deoxy-6,28-epoxy-23-(methoxyimino)-25-[(2*E*)-4-methylpent-2-en-1-yl]milbemycin B.

Ph Eur