*Preparation*: discs.

*Comparison*: *moxonidine CRS*.

TESTS

**Related substances**. Liquid chromatography (*2.2.29*).

*Test solution*. Dissolve 0.100 g of the substance to be examined in a mixture of equal volumes of *methanol R* and *water R* and dilute to 100.0 mL with the same mixture of solvents.

*Reference solution (a)*. Dissolve 10.0 mg of *moxonidine CRS* in a mixture of equal volumes of *methanol R* and *water R* and dilute to 10.0 mL with the same mixture of solvents.

*Reference solution (b)*. Dilute 1.0 mL of reference solution (a) to 100.0 mL with a mixture of equal volumes of *methanol R* and *water R*. Dilute 2.0 mL of this solution to 20.0 mL with a mixture of equal volumes of *methanol R* and *water R*.

*Reference solution (c)*. Dissolve 5.0 mg of *moxonidine impurity A CRS* in a mixture of equal volumes of *methanol R* and *water R* and dilute to 100.0 mL with the same mixture of solvents.

*Reference solution (d)*. Dilute 6.0 mL of reference solution (c) to 100.0 mL with a mixture of equal volumes of *methanol R* and *water R*.

*Reference solution (e)*. Dilute 2.5 mL of reference solution (a) to 50.0 mL with reference solution (c).

*Column*:

– *size*: *l* = 0.25 m, Ø = 4 mm;
– *stationary phase*: *base-deactivated octylsilyl silica gel for chromatography R* (5 µm);
– *temperature*: 40 °C.

*Mobile phase*: mix 136 volumes of *acetonitrile R* with 1000 volumes of a 3.48 g/L solution of *sodium pentanesulfonate R* previously adjusted to pH 3.5 with *dilute sulfuric acid R*.

*Flow rate*: 1.2 mL/min.

*Detection*: spectrophotometer at 230 nm.

*Injection*: 20 µL; inject a blank, the test solution and reference solutions (b), (d) and (e).

*Run time*: twice the retention time of moxonidine.

*Relative retentions* with reference to moxonidine (retention time = about 11.6 min): impurity A = about 0.9; impurity B = about 1.7.

*System suitability*: reference solution (e):

– *resolution*: minimum of 2 between the peaks due to impurity A and moxonidine.

*Limits*:

– *impurity A*: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (d) (0.3 per cent);
– *impurity B*: not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (b) (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 (b) (0.10 per cent);
– *total*: not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 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); disregard any peak observed with the blank run.

**Loss on drying** (*2.2.32*): maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C for 3 h.

**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.

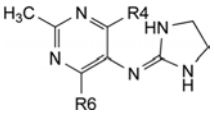
*Injection*: test solution and reference solution (a).

Calculate the percentage content of $C_9H_{12}ClN_5O$ from the areas of the peaks and the declared content of *moxonidine 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.*




A. R4 = R6 = Cl: 4,6-dichloro-*N*-(imidazolidin-2-ylidene)-2-methylpyrimidin-5-amine (6-chloromoxonidine),

B. R4 = R6 = $OCH_3$: *N*-(imidazolidin-2-ylidene)-4,6-dimethoxy-2-methylpyrimidin-5-amine (4-methoxymoxonidine),

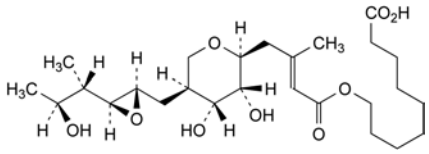
C. R4 = OH, R6 = $OCH_3$: 5-[(imidazolidin-2-ylidene)amino]-6-methoxy-2-methylpyrimidin-4-ol (4-hydroxymoxonidine),

D. R4 = OH, R6 = Cl: 6-chloro-5-[(imidazolidin-2-ylidene)amino]-2-methylpyrimidin-4-ol (6-desmethylmoxonidine).

**01/2008:1450**
**corrected 6.0**

# MUPIROCIN

## Mupirocinum




$C_{26}H_{44}O_9$ $M_r$ 500.6
[12650-69-0]

DEFINITION

9-[[(2*E*)-4-[(2*S*,3*R*,4*R*,5*S*)-3,4-Dihydroxy-5-[[(2*S*,3*S*)-3-[(1*S*,2*S*)-2-hydroxy-1-methylpropyl]oxiranyl]methyl]tetrahydro-2*H*-pyran-2-yl]-3-methylbut-2-enoyl]oxy]nonanoic acid.

Substance produced by the growth of certain strains of *Pseudomonas fluorescens* or obtained by any other means.

*Content*: 93.0 per cent to 102.0 per cent (anhydrous substance).

CHARACTERS

*Appearance*: white or almost white powder.

*Solubility*: slightly soluble in water, freely soluble in acetone, in anhydrous ethanol and in methylene chloride.

It shows polymorphism (*5.9*).

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

*Comparison*: *Ph. Eur. reference spectrum of mupirocin*.

TESTS

**pH** (*2.2.3*): 3.5 to 4.0 for a freshly prepared saturated solution (about 10 g/L) in *carbon dioxide-free water R*.

**Specific optical rotation** (*2.2.7*): – 17 to – 21 (anhydrous substance).

Dissolve 0.50 g in *methanol R* and dilute to 10.0 mL with the same solvent.

**Related substances**. Liquid chromatography (*2.2.29*).

*Solvent mixture.* Mix 50 volumes of *methanol R* and 50 volumes of a 13.6 g/L solution of *sodium acetate R* adjusted to pH 4.0 with *acetic acid R*.

*Test solution.* Dissolve 50.0 mg of the substance to be examined in the solvent mixture and dilute to 10.0 mL with the solvent mixture.

*Reference solution (a).* Dilute 1.0 mL of the test solution to 50.0 mL with the solvent mixture.

*Reference solution (b).* Adjust 10 mL of reference solution (a) to pH 2.0 with *hydrochloric acid R* and allow to stand for 20 h.

*Reference solution (c).* Dissolve 25 mg of *mupirocin lithium CRS* in the solvent mixture and dilute to 200.0 mL with the solvent mixture.

*Column*:

– *size*: *l* = 0.25 m, Ø = 4.6 mm;
– *stationary phase*: *octylsilyl silica gel for chromatography R* (5 µm).

*Mobile phase*: mix 20 volumes of *water R*, 30 volumes of *tetrahydrofuran R* and 50 volumes of a 10.5 g/L solution of *ammonium acetate R* adjusted to pH 5.7 with *acetic acid R*.

*Flow rate*: 1 mL/min.

*Detection*: spectrophotometer at 240 nm.

*Injection*: 20 µL.

*Run time*: 3.5 times the retention time of mupirocin.

*Relative retention* with reference to mupirocin: impurity C = about 0.75.

*System suitability*: reference solution (b):

– *resolution*: minimum 7.0 between the 2nd of the 2 peaks due to hydrolysis products and the peak due to mupirocin.

*Limits*:

– *impurity C*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (4 per cent);
– *any other impurity*: for each impurity, not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (1 per cent);
– *total*: not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (a) (6 per cent);
– *disregard limit*: 0.05 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent).

**Water** (*2.5.12*): maximum 1.0 per cent, determined on 0.500 g.

ASSAY

Liquid chromatography (*2.2.29*).

*Test solution.* Dissolve 25.0 mg of the substance to be examined in 5 mL of *methanol R* and dilute to 200.0 mL with a 7.5 g/L solution of *ammonium acetate R* adjusted to pH 5.7 with *acetic acid R*.

*Reference solution (a).* Dissolve 25.0 mg of *mupirocin lithium CRS* in 5 mL of *methanol R* and dilute to 200.0 mL with a 7.5 g/L solution of *ammonium acetate R* adjusted to pH 5.7 with *acetic acid R*.

*Reference solution (b).* Adjust 10 mL of the test solution to pH 2.0 with *hydrochloric acid R* and allow to stand for 20 h.

*Column*:

– *size*: *l* = 0.25 m, Ø = 4.6 mm;
– *stationary phase*: *octylsilyl silica gel for chromatography R* (5 µm).

*Mobile phase*: mix 19 volumes of *water R*, 32 volumes of *tetrahydrofuran R* and 49 volumes of a 10.5 g/L solution of *ammonium acetate R* adjusted to pH 5.7 with *acetic acid R*.

*Flow rate*: 1 mL/min.

*Detection*: spectrophotometer at 230 nm.

*Injection*: 20 µL.

*System suitability*:

– *resolution*: minimum 7.0 between the 2nd of the 2 peaks due to hydrolysis products and the peak due to mupirocin in the chromatogram obtained with reference solution (b);
– *repeatability*: maximum relative standard deviation of 1.0 per cent after 6 injections of reference solution (a).

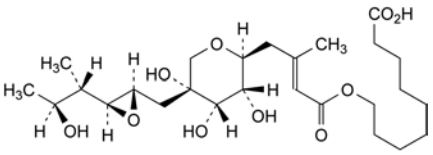
STORAGE

Protected from light.

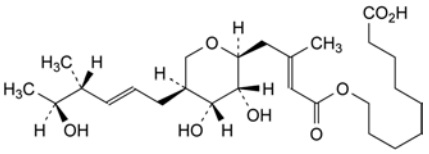
IMPURITIES

*Specified impurities*: *C*.

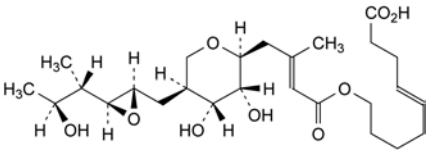
*Other detectable impurities* (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph *Substances for pharmaceutical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



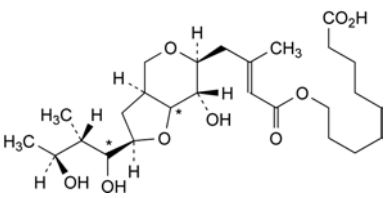
A. 9-[[(2*E*)-4-[(2*S*,3*R*,4*R*,5*R*)-3,4,5-trihydroxy-5-[[(2*S*,3*S*)-3-[(1*S*,2*S*)-2-hydroxy-1-methylpropyl]oxiranyl]methyl]-tetrahydro-2*H*-pyran-2-yl]-3-methylbut-2-enoyl]oxy]nonanoic acid (pseudomonic acid B),



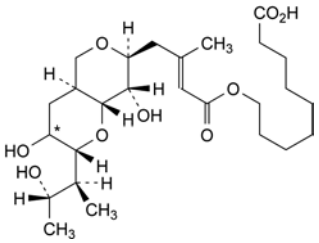
B. 9-[[(2*E*)-4-[(2*S*,3*R*,4*R*,5*S*)-3,4-dihydroxy-5-[(2*E*,4*R*,5*S*)-5-hydroxy-4-methylhex-2-enyl]tetrahydro-2*H*-pyran-2-yl]-3-methylbut-2-enoyl]oxy]nonanoic acid (pseudomonic acid C),



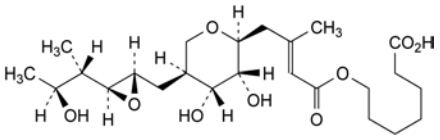
C. (4*E*)-9-[[(2*E*)-4-[(2*S*,3*R*,4*R*,5*S*)-3,4-dihydroxy-5-[[(2*S*,3*S*)-3-[(1*S*,2*S*)-2-hydroxy-1-methylpropyl]oxiranyl]methyl]-tetrahydro-2*H*-pyran-2-yl]-3-methylbut-2-enoyl]oxy]-non-4-enoic acid (pseudomonic acid D),



D. 9-[[(2*E*)-4-[(2*R*,3a*S*,6*S*,7*S*)-2-[(2*S*,3*S*)-1,3-dihydroxy-2-methylbutyl]-7-hydroxyhexahydro-4*H*-furo[3,2-*c*]pyran-6-yl]-3-methylbut-2-enoyl]oxy]nonanoic acid,



E. 9-[[(2*E*)-4-[(2*R*,3*RS*,4a*S*,7*S*,8*S*,8a*R*)-3,8-dihydroxy-2-[(1*S*,2*S*)-2-hydroxy-1-methylpropyl]hexahydro-2*H*,5*H*-pyrano[4,3-*b*]pyran-7-yl]-3-methylbut-2-enoyl]oxy]nonanoic acid,

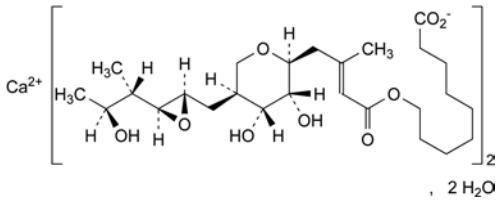


F. 7-[[(2*E*)-4-[(2*S*,3*R*,4*R*,5*S*)-3,4-dihydroxy-5-[[(2*S*,3*S*)-3-[(1*S*,2*S*)-2-hydroxy-1-methylpropyl]oxiranyl]methyl]tetrahydro-2*H*-pyran-2-yl]-3-methylbut-2-enoyl]oxy]heptanoic acid.

**07/2010:1451**

# MUPIROCIN CALCIUM

## Mupirocinum calcicum



$C_{52}H_{86}CaO_{18},2H_2O$ $M_r$ 1075

[115074-43-6]

DEFINITION

Calcium bis[9-[[(2*E*)-4-[(2*S*,3*R*,4*R*,5*S*)-3,4-dihydroxy-5-[[(2*S*,3*S*)-3-[(1*S*,2*S*)-2-hydroxy-1methylpropyl]oxiranyl]-methyl]tetrahydro-2*H*-pyran-2-yl]-3-methylbut-2-enoyl]-oxy]nonanoate] dihydrate.

Substance produced by the growth of certain strains of *Pseudomonas fluorescens* or obtained by any other means.

*Content*: 93.0 per cent to 102.0 per cent (anhydrous substance).

CHARACTERS

*Appearance*: white or almost white powder.

*Solubility*: very slightly soluble in water, sparingly soluble in anhydrous ethanol and in methylene chloride.

IDENTIFICATION

A. Infrared absorption spectrophotometry (*2.2.24*).

*Comparison*: *Ph. Eur. reference spectrum of mupirocin calcium.*

B. It gives reaction (a) of calcium (*2.3.1*).

TESTS

**Specific optical rotation** (*2.2.7*): – 16 to – 20 (anhydrous substance).

Dissolve 0.50 g in *methanol R* and dilute to 10.0 mL with the same solvent.

**Related substances**. Liquid chromatography (*2.2.29*).

*Solvent mixture.* Mix 50 volumes of *methanol R* and 50 volumes of a 13.6 g/L solution of *sodium acetate R* adjusted to pH 4.0 with *acetic acid R*.

*Test solution.* Dissolve 50.0 mg of the substance to be examined in the solvent mixture and dilute to 10.0 mL with the solvent mixture.

*Reference solution (a).* Dilute 1.0 mL of the test solution to 50.0 mL with the solvent mixture.

*Reference solution (b).* Adjust 10 mL of reference solution (a) to pH 2.0 with *hydrochloric acid R* and allow to stand for 20 h.

*Reference solution (c).* Dissolve 25 mg of *mupirocin lithium CRS* in the solvent mixture and dilute to 200.0 mL with the solvent mixture.

*Column*:

– *size*: *l* = 0.25 m, Ø = 4.6 mm;
– *stationary phase*: *octylsilyl silica gel for chromatography R* (5 µm).

*Mobile phase*: mix 20 volumes of *water R*, 30 volumes of *tetrahydrofuran R* and 50 volumes of a 10.5 g/L solution of *ammonium acetate R* adjusted to pH 5.7 with *acetic acid R*.

*Flow rate*: 1 mL/min.

*Detection*: spectrophotometer at 240 nm.

*Injection*: 20 µL.

*Run time*: 3.5 times the retention time of mupirocin.

*Relative retention* with reference to mupirocin: impurity C = about 0.75.

*System suitability*: reference solution (b):

– *resolution*: minimum 7.0 between the 2nd of the 2 peaks due to hydrolysis products and the peak due to mupirocin.

*Limits*:

– *impurity C*: not more than 1.25 times the area of the principal peak in the chromatogram obtained with reference solution (a) (2.5 per cent);
– *any other impurity*: for each impurity, not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (1 per cent);
– *total*: not more than 2.25 times the area of the principal peak in the chromatogram obtained with reference solution (a) (4.5 per cent);
– *disregard limit*: 0.05 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent).

**Chlorides** (*2.4.4*): maximum 0.5 per cent.

Dissolve 10.0 mg in a mixture of 1 mL of *dilute nitric acid R* and 15 mL of *methanol R*.

**Water** (*2.5.12*): 3.0 per cent to 4.5 per cent, determined on 0.500 g.

ASSAY

Liquid chromatography (*2.2.29*).

*Test solution.* Dissolve 25.0 mg of the substance to be examined in 5 mL of *methanol R* and dilute to 200.0 mL with a 7.5 g/L solution of *ammonium acetate R* adjusted to pH 5.7 with *acetic acid R*.

*Reference solution (a).* Dissolve 25.0 mg of *mupirocin lithium CRS* in 5 mL of *methanol R* and dilute to 200.0 mL with a 7.5 g/L solution of *ammonium acetate R* adjusted to pH 5.7 with *acetic acid R*.

*Reference solution (b).* Adjust 10 mL of the test solution to pH 2.0 with *hydrochloric acid R* and allow to stand for 20 h.

*Column*:

– *size*: *l* = 0.25 m, Ø = 4.6 mm;
– *stationary phase*: *octylsilyl silica gel for chromatography R* (5 µm).

*Mobile phase*: mix 19 volumes of *water R*, 32 volumes of *tetrahydrofuran R* and 49 volumes of a 10.5 g/L solution of *ammonium acetate R* adjusted to pH 5.7 with *acetic acid R*.

*Flow rate*: 1 mL/min.

*Detection*: spectrophotometer at 230 nm.

*Injection*: 20 µL.