Column:

– *size*: *l* = 0.25 m, Ø = 4.6 mm;

– *stationary phase*: *base-deactivated octylsilyl silica gel for chromatography R* (5 µm);

– *temperature*: 40 °C.

Mobile phase: *acetonitrile R*, solution B (45:55 *V/V*).

Flow rate: 1.0 mL/min.

Detection: spectrophotometer at 260 nm.

Injection: 10 µL.

Run time: twice the retention time of indinavir.

Retention time: indinavir = about 10 min.

Calculate the percentage content of $C_{36}H_{49}N_5O_8S$ using the declared content of *indinavir CRS* and multiplying by a correction factor of 1.1598.

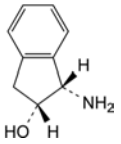
STORAGE

In an airtight container, protected from light.

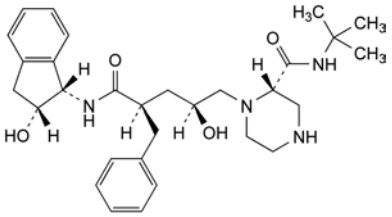
IMPURITIES

Specified impurities: A, B, C, D, E.

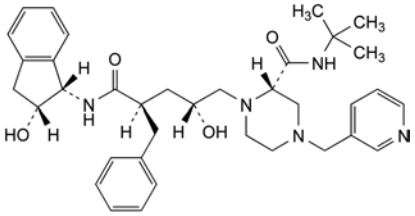
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph *Substances for pharmaceutical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



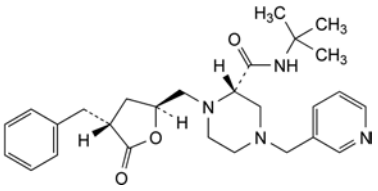
A. (1*S*,2*R*)-1-amino-2,3-dihydro-1*H*-inden-2-ol (*cis*-aminoindanol),



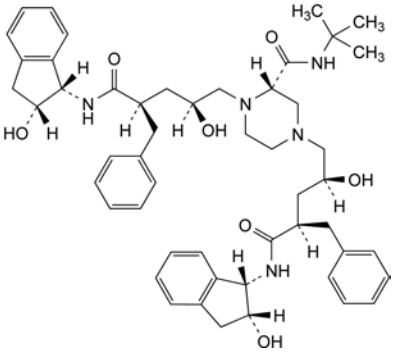
B. (2*S*)-1-[(2*S*,4*R*)-4-benzyl-2-hydroxy-5-[[(1*S*,2*R*)-2-hydroxy-2,3-dihydro-1*H*-inden-1-yl]amino]-5-oxopentyl]-*N*-(1,1-dimethylethyl)piperazine-2-carboxamide,



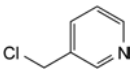
C. (2*S*)-1-[(2*R*,4*R*)-4-benzyl-2-hydroxy-5-[[(1*S*,2*R*)-2-hydroxy-2,3-dihydro-1*H*-inden-1-yl]amino]-5-oxopentyl]-*N*-(1,1-dimethylethyl)-4-(pyridin-3-ylmethyl)piperazine-2-carboxamide,



D. (3*R*,5*S*)-3-benzyl-5-[[(2*S*)-2-[(1,1-dimethylethyl)carbamoyl]-4-(pyridin-3-ylmethyl)piperazin-1-yl]methyl]-4,5-dihydrofuran-2(3*H*)-one,



E. (2*S*)-1,4-bis[(2*S*,4*R*)-4-benzyl-2-hydroxy-5-[[(1*S*,2*R*)-2-hydroxy-2,3-dihydro-1*H*-inden-1-yl]amino]-5-oxopentyl]-*N*-(1,1-dimethylethyl)piperazine-2-carboxamide,

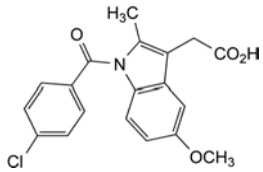


F. 3-(chloromethyl)pyridine (nicotinyl chloride).

01/2008:0092
corrected 6.0

INDOMETACIN

Indometacinum



$C_{19}H_{16}ClNO_4$ M_r 357.8
[53-86-1]

DEFINITION

Indometacin contains not less than 98.5 per cent and not more than the equivalent of 100.5 per cent of [1-(4-chlorobenzoyl)-5-methoxy-2-methylindol-3-yl]acetic acid, calculated with reference to the dried substance.

CHARACTERS

A white or yellow, crystalline powder, practically insoluble in water, sparingly soluble in alcohol.

IDENTIFICATION

First identification: A, C.

Second identification: A, B, D, E.

A. Melting point (*2.2.14*): 158 °C to 162 °C.

B. Dissolve 25 mg in a mixture of 1 volume of *1 M hydrochloric acid* and 9 volumes of *methanol R* and dilute to 100.0 mL with the same mixture of solvents. Dilute 10.0 mL of the solution to 100.0 mL with a mixture of 1 volume of *1 M hydrochloric acid* and 9 volumes of *methanol R*. Examined between 300 nm and 350 nm (*2.2.25*), the solution shows an absorption maximum at 318 nm. The specific absorbance at the maximum is 170 to 190.

C. Examine by infrared absorption spectrophotometry (*2.2.24*), comparing with the spectrum obtained with *indometacin CRS*. Examine the substances in the solid state without recrystallisation.

D. Dissolve 0.1 g in 10 mL of *alcohol R*, heating slightly if necessary. To 0.1 mL of the solution add 2 mL of a freshly prepared mixture of 1 volume of a 250 g/L solution of *hydroxylamine hydrochloride R* and 3 volumes of *dilute sodium hydroxide solution R*. Add 2 mL of *dilute hydrochloric acid R* and 1 mL of *ferric chloride solution R2* and mix. A violet-pink colour develops.

E. To 0.5 mL of the solution in alcohol prepared in identification test D, add 0.5 mL of *dimethylaminobenzaldehyde solution R2*. A precipitate is formed that dissolves on shaking. Heat on a water-bath. A bluish-green colour is produced. Continue to heat for 5 min and cool in iced water for 2 min. A precipitate is formed and the colour changes to light greyish-green. Add 3 mL of *alcohol R*. The solution is clear and violet-pink in colour.

TESTS

Related substances. Examine by thin-layer chromatography (*2.2.27*), using *silica gel HF_{254} R* as the coating substance. Prepare the slurry using a 46.8 g/L solution of *sodium dihydrogen phosphate R*.

Test solution. Dissolve 0.2 g of the substance to be examined in *methanol R* and dilute to 10 mL with the same solvent. Prepare immediately before use.

Reference solution. Dilute 1 mL of the test solution to 200 mL with *methanol R*.

Apply separately to the plate 10 µL of each solution. Develop over a path of 15 cm using a mixture of 30 volumes of *light petroleum R* and 70 volumes of *ether R*. Allow the plate to dry in air and examine in ultraviolet light at 254 nm. Any spot in the chromatogram obtained with the test solution, apart from the principal spot, is not more intense than the spot in the chromatogram obtained with the reference solution (0.5 per cent).

Heavy metals (*2.4.8*). 2.0 g complies with limit test C for heavy metals (20 ppm). Prepare the standard using 4 mL of *lead standard solution (10 ppm Pb) R*.

Loss on drying (*2.2.32*). Not more than 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C.

Sulfated ash (*2.4.14*). Not more than 0.1 per cent, determined on 1.0 g.

ASSAY

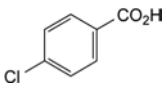
Dissolve 0.300 g in 75 mL of *acetone R*, through which *nitrogen R*, free from carbon dioxide, has been passed for 15 min. Maintain a constant stream of nitrogen through the solution. Add 0.1 mL of *phenolphthalein solution R*. Titrate with *0.1 M sodium hydroxide*. Carry out a blank titration.

1 mL of *0.1 M sodium hydroxide* is equivalent to 35.78 mg of $C_{19}H_{16}ClNO_4$.

STORAGE

Store protected from light.

IMPURITIES

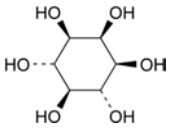


A. 4-chlorobenzoic acid.

01/2008:1805
corrected 7.0

myo-INOSITOL

myo-Inositolum



$C_6H_{12}O_6$ M_r 180.2
[87-89-8]

DEFINITION

Cyclohexane-1,2,3,5/4,6-hexol.

Content: 97.0 per cent to 102.0 per cent (anhydrous substance).

CHARACTERS

Appearance: white or almost white, crystalline powder.

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

IDENTIFICATION

A. Infrared absorption spectrophotometry (*2.2.24*).
Comparison: *myo-inositol CRS*.

B. Examine the chromatograms obtained in the assay.
Results: the principal peak in the chromatogram obtained with the test solution is similar in retention time and size to the principal peak in the chromatogram obtained with reference solution (a).

TESTS

Solution S. Dissolve 10.0 g in *distilled water R* and dilute to 100.0 mL with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and colourless (*2.2.2, Method II*).

Conductivity (*2.2.38*): maximum 30 µS·cm^{-1}.

Dissolve 10.0 g in *carbon dioxide-free water R* prepared from *distilled water R*, with gentle warming if necessary, and dilute to 50.0 mL with the same solvent. Measure the conductivity of the solution while gently stirring with a magnetic stirrer.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 0.500 g of the substance to be examined in *water R* and dilute to 10.0 mL with the same solvent.

Reference solution (a). Dissolve 0.500 g of *myo-inositol CRS* in *water R* and dilute to 10.0 mL with the same solvent.

Reference solution (b). Dilute 2.0 mL of the test solution to 100.0 mL with *water R*. Dilute 5.0 mL of this solution to 100.0 mL with *water R*.

Reference solution (c). Dissolve 0.5 g of *myo-inositol R* and 0.5 g of *mannitol R* in *water R* and dilute to 10 mL with the same solvent.

Column:
- *size*: *l* = 0.3 m, Ø = 7.8 mm;
- *stationary phase*: *strong cation exchange resin (calcium form) R* (9 µm);
- *temperature*: 85 °C.

Mobile phase: *water R*.

Flow rate: 0.5 mL/min.

Detection: refractometer maintained at a constant temperature (at about 30-35 °C for example).

Injection: 20 µL of the test solution and reference solutions (b) and (c).

Run time: twice the retention time of *myo*-inositol.