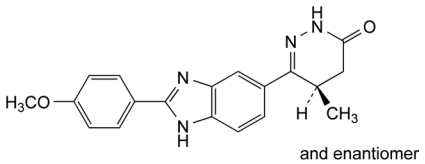
01/2008:2179

PIMOBENDAN

Pimobendanum



and enantiomer

$C_{19}H_{18}N_4O_2$ M_r 334.4
[74150-27-9]

DEFINITION

(5*RS*)-6-[2-(4-Methoxyphenyl)-1*H*-benzimidazol-5-yl]-5-methyl-4,5-dihydropyridazin-3(2*H*)-one.

Content: 98.0 per cent to 101.0 per cent (anhydrous substance).

CHARACTERS

Appearance: white or slightly yellowish powder, hygroscopic.

Solubility: practically insoluble in water, freely soluble in dimethylformamide, slightly soluble in acetone and in methanol.

mp: about 242 °C.

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *pimobendan CRS*.

TESTS

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 50 mg of the substance to be examined in *methanol R* and dilute to 10.0 mL with the same solvent.

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

Reference solution (b). Dissolve the contents of a vial of *pimobendan for system suitability CRS* (impurities A and B) in 1.0 mL of *methanol R*.

Column:

- *size*: *l* = 0.125 m, Ø = 4.6 mm,
- *stationary phase*: spherical *end-capped octadecylsilyl silica gel for chromatography R1* (5 µm),
- *temperature*: 45 °C.

Mobile phase:

- *mobile phase A*: dissolve 3.0 g of *potassium dihydrogen phosphate R* in 950 mL of *water for chromatography R*, adjust to pH 2.5 with *dilute phosphoric acid R* and dilute to 1000 mL with *water for chromatography R*,
- *mobile phase B*: *acetonitrile for chromatography R*,

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 6	85 → 80	15 → 20
6 - 20	80 → 20	20 → 80
20 - 20.1	20 → 85	80 → 15
20.1 - 30	85	15

Flow rate: 1 mL/min.

Detection: spectrophotometer at 290 nm.

Injection: 10 µL.

Relative retention with reference to pimobendan (retention time = about 8.3 min): impurity A = about 1.3; impurity B = about 1.4.

System suitability: reference solution (b):

- *resolution*: minimum 2.0 between the peaks due to impurity A and impurity B.

Limits:

- *impurities A, B*: for each impurity, not more than 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent),
- *any other impurity*: for each impurity, not more than 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent),
- *total*: not more than 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent),
- *disregard limit*: 0.05 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Heavy metals (*2.4.8*): maximum 10 ppm.

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

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

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

ASSAY

Dissolve 0.250 g in 5 mL of *anhydrous formic acid R*. Add 10 mL of *acetic anhydride R* and 70 mL of *anhydrous acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

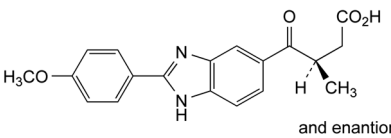
1 mL of *0.1 M perchloric acid* is equivalent to 33.44 mg of $C_{19}H_{18}N_4O_2$.

STORAGE

In an airtight container.

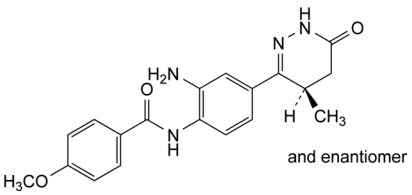
IMPURITIES

Specified impurities: A, B.



and enantiomer

A. (3*RS*)-4-[2-(4-methoxyphenyl)-1*H*-benzimidazol-5-yl]-3-methyl-4-oxobutanoic acid,



and enantiomer

B. *N*-[2-amino-4-[(4*RS*)-4-methyl-6-oxo-1,4,5,6-tetrahydropyridazin-3-yl]phenyl]-4-methoxybenzamide.