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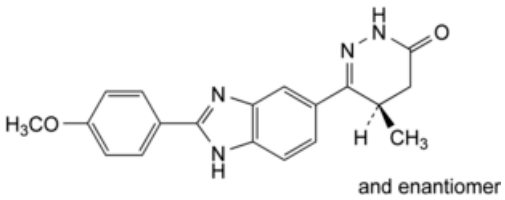
Edition: BP 2025 (Ph. Eur. 11.6 update)

Pimobendan

General Notices

(Pimobendan for Veterinary Use, Ph Eur monograph 2179)



$C_{19}H_{18}N_4O_2$ 334.4 *74150-27-9*

Action and use

Inhibitor of phosphodiesterase type III; calcium sensitizer.

Preparation

Pimobendan Capsules

Ph Eur

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, hygroscopic powder.

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. Dilute 2.0 mL of this solution to 10.0 mL with methanol R.

Reference solution (b) Dissolve the contents of a vial of pimobendan for system suitability CRS (containing impurities A and B) in 1 mL of methanol R.

Column:

— *size*: *l* = 0.125 m, Ø = 4.6 mm;

— *stationary phase*: base-deactivated end-capped octadecylsilyl silica gel for chromatography R (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 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

Flow rate 1 mL/min.

Detection Spectrophotometer at 290 nm.

Injection 10 µL.

Identification of impurities Use the chromatogram obtained with reference solution (b) to identify the peaks due to impurities A and B.

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 impurities A and B.

Limits:

— *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.20 per cent);

— *total*: not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent);

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— *disregard limit*: 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.10 per cent).

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*).

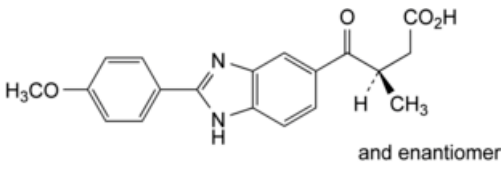
1 mL of *0.1 M perchloric acid* is equivalent to 33.44 mg of $C_{19}H_{18}N_4O_2$.

STORAGE

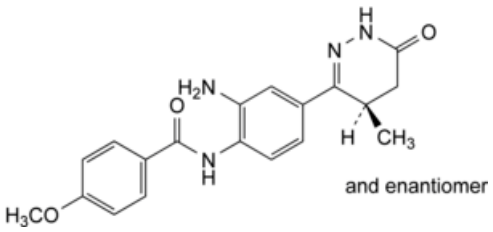
In an airtight container.

IMPURITIES

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.*



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



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