Pimobendan

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Manufacturers, regulatory authorities, health authorities, researchers, and other stakeholders are invited to provide their feedback and comments on this draft proposal. Manufacturers are also invited to submit samples of their products to the IPC to ensure that the proposed monograph adequately controls the quality of the product(s) they manufacture. Comments and samples received after the last date will not be considered by the IPC before finalizing the monograph.

Please send any comments you may have on this draft document to lab.ipc@gov.in, with a copy to Dr. Gaurav Pratap Singh (email: gpsingh.ipc@gov.in) before the last date for comments.

Document History and Schedule for the Adoption Process

Description	Details
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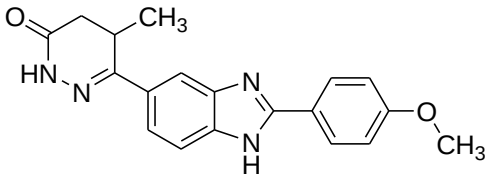
Further follow-up action as required.	

Pimobendan



$C_{19}H_{18}N_4O_2$ Mol Wt. 334.4

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

Pimobendan contains not less than 98.0 per cent and not more than 101.0 per cent of $C_{19}H_{18}N_4O_2$, calculated on the anhydrous basis.

Category. Inhibitor of phosphodiesterase type III; calcium sensitizer.

Description. A white or slightly yellowish, hygroscopic powder.

Identification

Determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *pimobendan IPRS* or with the reference spectrum of pimobendan.

Tests

Melting point (2.4.21). About 242°.

Related substances. A. Determine by liquid chromatography (2.4.14).

Test solution. Dissolve 50 mg of the substance under examination in *methanol* and dilute to 10.0 ml with *methanol*.

Reference solution (a). A 0.001 per cent w/v solution of *pimobendan IPRS* in *methanol.*

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

Chromatographic system
- a stainless steel column 12.5 cm x 4.6 mm, packed with base deactivated end capped octadecylsilane bonded to porous silica (5 µm),
- column temperature: 45º,
- mobile phase A: a buffer solution prepared by dissolving 3 g of *potassium dihydrogen phosphate* in 1000 ml of *water*, adjusted to pH 2.5 with *dilute orthophosphoric acid*,
  B: *acetonitrile*,
- a gradient programme using the conditions given below,
- flow rate: 1 ml per minute,
- spectrophotometer set at 290 nm,
- injection volume: 10 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	85	15
6	80	20
20	20	80
20.1	85	15
25	85	15

	retention time
Pimobendan (retention time: about 8.3 minutes)	1.0
Pimobendan impurity A [1]	1.3
Pimobendan impurity B [2]	1.4

[1](3*RS*)-4-[2-(4-methoxyphenyl)-1*H*-benzimidazol-5-yl]-3-methyl-4-oxobutanoic acid,
[2](5*RS*)-6-[3-amino-4-(4-methoxybenzamido)phenyl]-5-methyl-4,5-dihydropyridazin-3(2*H*)-one.

Inject reference solution (b). The test is not valid unless the resolution between the peaks due to pimobendan impurity A and pimobendan impurity B is not less than 2.0.

Inject reference solution (a) and the test solution. In the chromatogram obtained with the test solution, the area of any other secondary peak is not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent) and the sum of areas of all the secondary peaks is not more the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent). Ignore any peak with an area less than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent).

Heavy metals (2.3.13). 1.0 g complies with the limit test for heavy metals, Method D (20 ppm). ~~Using 2.0 ml of *lead standard solution (10 ppm Pb).*~~

Sulphated ash (2.3.18). Not more than 0.1 per cent.

Water (2.3.43). Not more than 1.0 per cent, determined on 0.5 g.

Assay. Dissolve 0.25 g of the substance under examination in 5 ml of *anhydrous formic acid*. Add 10 ml of *acetic anhydride* and 70 ml of *anhydrous acetic acid*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (2.4.25). Carry out a blank titration.

1 ml of *0.1 M perchloric acid* is equivalent to 0.03344 g of $C_{19}H_{18}N_4O_2$.

Storage. Store protected from light at a temperature not exceeding 30°.

Pimobendan:

Solubility: Practically insoluble in *water*, freely soluble in *dimethylformamide*, slightly soluble in a*cetone* and in *methanol*.