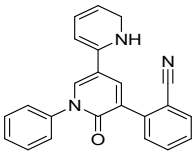
Perampanel



$C_{23}H_{15}N_3O.\ 3/4H_2O$ Mol. Wt. 362.9

Perampanel is 2-(2-oxo-1-phenyl-5-pyridin-2-yl-1,2-dihydropyridin-3-yl)benzonitrile hydrate.

Perampanel contains not less than 98.0 per cent and not more than 102.0 per cent of $C_{23}H_{15}N_3O$, calculated on the anhydrous basis.

Category. Antiepileptic.

Description. A white to yellowish white powder.

Identification

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

B. In the Assay, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with the reference solution (b).

Tests

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. 40 volumes of *acetonitrile* and 60 volumes of *water*.

Test solution. Dissolve 100 mg of the substance under examination in the mobile phase B and dilute to 50.0 ml with the mobile phase B. Dilute 1.0 ml of the solution to 10.0 ml with the solvent mixture.

Reference solution (a). A 0.2 per cent w/v solution of *perampanel IPRS* in mobile phase B.

Reference solution (b). Dilute 1.0 ml of reference solution (a) to 10.0 ml with the solvent mixture.

Reference solution (c). Dilute 1.0 ml of reference solution (b) to 100.0 ml with the solvent mixture.

Reference solution (d). A 0.01 per cent w/v solution of *perampanel impurity F IPRS (methyl 2-(2-oxo-1-phenyl-5-pyridin-2-yl-1,2-dihydropyridin-3-yl)benzoate)* in mobile phase B. Transfer 1.0 ml of the solution to a 50-ml volumetric flask, add 5.0 ml of reference solution (a) and dilute to volume with the solvent mixture.

Reference solution (e). A solution containing 0.01 per cent w/v, each of, *perampanel impurity A IPRS*, *perampanel impurity B IPRS*, *perampanel impurity C IPRS*, *perampanel impurity D IPRS* and *perampanel impurity E IPRS*, in mobile phase B. Transfer 1.0 ml of the solution to a 50-ml volumetric flask, add 5.0 ml of reference solution (a) and dilute to volume with solvent mixture.

Chromatographic system
- a stainless steel column 15 cm × 4.6 mm, packed with octadecylsilane bonded to porous silica (3.5 µm) (Such as Symmetry Shield RP 18),
- column temperature: 35°,
- mobile phase: A. 0.1 per cent w/v solution of *ammonium acetate* in a mixture of 90 volumes of *water* and 10 volumes of *acetonitrile,*

B. 0.1 per cent w/v solution of *ammonium acetate* in a mixture of 10 volumes of *water* and 90 volumes of *acetonitrile,*

- flow rate: 1 ml per minute,
- a gradient programme using the conditions given below,
- 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	60	40
15	60	40
25	0	100
35	0	100
45	60	40
50	60	40

Name	Relative retention time	Correction factor
Perampanel impurity A[1]	0.32	0.69
Perampanel impurity B[2]	0.75	0.92
Perampanel	1.0	--
Perampanel impurity C[3]	1.47	--
Perampanel impurity D[4]	1.64	1.37
Perampanel impurity E[5]	1.69	1.18

[1]1-Phenyl-5-pyridin-2-yl-2(*1H*)-pyridone
[2]3-Bromo-1-phenyl-5-pyridin-2-yl-2(*1H)*-pyridone
[3]3-(2-Oxo-1-phenyl-5-pyridin-2-yl-1,2-dihydropyridin-3-yl)benzonitrile
[4]2-Bromo-6-(2-oxo-1-phenyl-5-pyridin-2-yl-1,2-dihydropyridin-3-yl)benzonitrile
[5]3-(2-Oxo-1-phenyl-5-pyridin-2-yl-1,2-dihydropyridin-3-yl)-1,1'-biphenyl-2,2'-dicarbonitrile.

Inject reference solution (e) to identify the peaks due to perampanel impurity A, B, C, D and E.

Inject reference solution (d). The test is not valid unless the resolution between the peaks due to perampanel and perampanel impurity F is not less than 1.5, the column efficiency is not less than 8000 theoretical plates, the tailing factor is not more than 2.0.

Inject reference solution (c) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to perampanel impurity A, perampanel impurity B, perampanel impurity C and perampanel impurity D, each of, is not more than 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.1per cent). the area of any peak corresponding to perampanel impurity E is not more than 0.15 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.15 per cent), the area of any other secondary peak is not more than 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.1 per cent) and the sum of the areas of all the secondary peaks is not more than 0.5 times the area of the principal peak in the chromatogram with reference solution (c) (0.5 per cent). Ignore any peak with an area less than 0.05 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.05 per cent).

Heavy metals (2.3.13). 1.0 g complies with limit test for heavy metals, Method B (20 ppm).

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

Water (2.3.43). 3.5 per cent to 4.2 per cent.

Microbial contamination (2.2.9). Total aerobic microbial count is not more than 1000 CFU/g and total combined molds and yeasts is not more than 100 CFU/g. 1 g is free from, each of, *Staphylococcus aureus, Pseudomonas aeruginosa and Escherichia coli.*

Assay. Determine by liquid chromatography (2.4.14), as described under Related substances.

Inject reference solution (b). The test is not valid unless the relative standard deviation for replicate injections is not more than 1.0 per cent.

Inject reference solution (b) and the test solution.

Calculate the content of $C_{23}H_{15}N_3O$.

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