Azilsartan Kamedoxomil Tablets

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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

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Further follow-up action as required.	

Azilsartan Kamedoxomil Tablets

Azilsartan Kamedoxomil Tablets contain equivalent to not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of azilsartan medoxomil, $C_{30}H_{24}N_4O_8$.

Usual strengths. 20 mg; 40 mg; 80 mg.

Identification

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.

Tests

Dissolution (2.5.2).

Apparatus No. 2 (Paddle),
Medium. 900 ml of a phosphate buffer pH 7.8, prepared by dissolving 6.8 g of *potassium dihydrogen orthophosphate* in 1000 ml of *water*, adjusted to pH to 7.8 with *1 M sodium hydroxide*,
Speed and time. 50 rpm and 45 minutes.

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14).

Test solution. Dilute a suitable volume of the filtrate with the mobile phase, to obtain a solution containing 0.00022 per cent w/v of azilsartan medoxomil.

Reference solution. A 0.094 per cent w/v solution of *azilsartan kamedoxomil IPRS* in the *acetonitrile*. Dilute 5.0 ml of the solution to 200.0 ml with the dissolution medium. Dilute 2.0 ml of the solution to 20.0 ml with the mobile phase.

Chromatographic system
- – a stainless steel column 15 cm × 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm), (Such as Hypersil BDS C18),
- sampler temperature: 6°,
- mobile phase: a mixture of 45 volumes of a buffer solution prepared by dissolving 1.36 g of *potassium dihydrogen phosphate monohydrate* in 1000 ml of *water*, adjusted to pH 2.4 with *orthophosphoric acid* and 55 volumes of acetonitrile,
- flow rate: 1 ml per minute,
- spectrophotometer set at 220 nm,
- injection volume: 50 µl.

Inject the reference solution. The test is not valid unless the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of $C_{30}H_{24}N_4O_8$ in the medium, by multiplying the content of $C_{30}H_{23}KN_4O_8$ by 0.9372.

Q. Not less than 70 per cent of the stated amount of $C_{30}H_{24}N_4O_8$.

Related substances. Determine by liquid chromatography (2.4.14).

Test solution. Disperse a quantity of powdered tablets containing 80 mg of Azilsartan medoxomil in *acetonitrile*, with the aid of magnetic stirrer for 10 minutes and dilute to 100.0 ml with *acetonitrile*, filter.

Reference solution. A 0.00216 per cent w/v solution of *azilsartan kamedoxomil IPRS* in *acetonitrile*. Dilute 1.0 ml of the solution to 10.0 ml with *acetonitrile*

Chromatographic system
- a stainless steel column 15 cm × 4.6 mm, packed with octadecylsilane bonded to porous silica (3.5 µm) (Such as Sunfire C18),
- sample temperature: 5°,
- mobile phase: A. a buffer solution prepared by dissolving 1.36 g of *potassium dihydrogen orthophosphate* in 1000 ml of *water* and adjusted to pH 3.5 with orthophosphoric acid,
  B. a mixture of 30 volumes of mobile phase A and 70 volumes of *acetonitrile*,
- flow rate: 0.8 ml per minute,
- a gradient programme using the conditions given below,
- spectrophotometer set at 220 nm,
- injection volume: 10 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	40	60
5	40	60
40	20	80
45	20	80
50	40	60
60	40	60

The relative retention time with reference to azilsartan medoxomil, for azilsartan kamedoxomil impurity B is about 0.34.

Inject the reference solution. The test is not valid unless the column efficiency is not less than 2000 theoretical plates, the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 5.0 per cent.

Inject the reference solution and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to azilsartan kamedoxomil impurity B [(2-Ethoxy-1-{[2'-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)biphenyl-4-yl]methyl}-1H-benzo[d]imidazole-7-carboxylic acid] is not more than 12 times the area of the principal peak in the chromatogram obtained with the reference solution (3.0 per cent), the area of any other secondary peak is not more than twice the area of the principal peak in the chromatogram obtained with the reference solution (0.5 per cent) and the sum of the areas of all the secondary peaks is not more than 16 times the area of the principal peak in the chromatogram obtained with reference solution (b) (4.0 per cent).

Other tests. Comply with the tests stated under Tablets.

Assay. Determine by liquid chromatography (2.4.14), as described under Dissolution with the following modifications.

Test solution. Weigh and powder 20 tablets. Disperse a quantity of powdered tablets containing 50 mg of Azilsartan medoxomil in the mobile phase, with the aid of ultrasound for 5 minutes and dilute to 100.0 ml with the mobile phase, filter.

NOTE- sonicator bath temperature should not exceed 10°.

Reference solution. A 0.0053 per cent w/v solution of *azilsartan kamedoxomil IPRS* in the mobile phase.

- injection volume: 20 µl.

Inject the reference solution. The test is not valid unless the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of $C_{30}H_{24}N_4O_8$ in the tablets.

1 mg of azilsartan kamedoxomil, $C_{30}H_{23}KN_4O_8$ is equivalent to 0.9372 mg of azilsartan medoxomil, $C_{30}H_{24}N_4O_8$.

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