Brivaracetam Injection

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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.	

Brivaracetam Injection

Brivaracetam Injection is a sterile solution of Brivaracetam in Water for Injections.

Brivaracetam Injection contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of brivaracetam, $C_{11}H_{20}N_2O_2$.

Usual strength. 10 mg per ml.

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.

Test

pH (2.4.24). 4.5 to 6.5.

Related substances. Determine by liquid chromatography (2.4.14).

Test solution. Dilute a volume of the injection containing 50 mg of Brivaracetam to 50.0 ml with mobile phase A.

Reference solution (a). A 0.0003 per cent w/v solution of *brivaracetam IPRS* in mobile phase A.

Reference solution (b). Dilute 3.0 ml of reference solution (a) to 10.0 ml with mobile phase A.

Chromatographic system
- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica, modified with pentafluorophenyl (5µm) (Such as ACE C18-PFP),
- sample temperature:10°,
- column temperature: 35°,
- mobile phase: A. a 0.1 per cent v/v solution of *orthophosphoric acid* in *water*.
  B. a mixture of 40 volumes of mobile phase A, 30 volumes of *acetonitrile* and 30 volumes of *methanol*,
- a gradient programme using the conditions given below,
- flow rate: 1 ml per minute,
- spectrophotometer set at 210 nm,
- injection volume: 15 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0.01	100	0
5	100	0
20	50	50
50	50	50
50.1	100	0
60	100	0

The retention time of brivaracetam peak is about 29 minutes.

Inject reference solution (a) and (b). The test is not valid unless the column efficiency is not less than 10000 theoretical plates, the tailing factor is not more than 2.0, the relative standard deviation for replicate injections is not more than 10.0 per cent in the chromatogram obtained with reference solution (a) and the signal to noise ratio for the principal peak is not less than 10 in the chromatogram obtained with reference solution (b).

Inject reference solution (a) and the test solution. In the chromatogram obtained with the test solution, the area of any secondary peak is not more than 1.67 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent) and the sum of the area of all the secondary peaks is not more than 6.67 times the area of the principal peak in the chromatogram obtained with reference solution (a) (2.0 per cent). Ignore any peak with an area less than 0.17 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Bacterial endotoxins (2.2.3). Not more than 2 Endotoxin Units per mg of brivaracetam.

Sterility (2.2.11). Complies with the test for sterility.

Other tests. Comply with the tests stated under Parenteral Preparations (Injections).

Assay. Determine by liquid chromatography (2.4.14).

Buffer solution. A 0.1 per cent v/v solution of *orthophosphoric acid* in *water*.

Test solution. Dilute a volume of the injection containing 50 mg of Brivaracetam to 250.0 ml with the buffer solution.

Reference solution. A 0.02 per cent w/v solution of *brivaracetam IPRS* in the buffer solution.

Chromatographic system
- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica, modified with pentafluorophenyl (5µm) (Such as ACE C18-PFP),
- column temperature: 35°,
- mobile phase: a mixture of 64 volumes of the buffer solution, 18 volumes of *acetonitrile* and 18 volumes of *methanol*,
- flow rate: 1 ml per minute,
- spectrophotometer set at 210 nm,
- injection volume: 15 µl.

The retention time of brivaracetam peak is about 8 minutes.

Inject the reference solution. The test is not valid unless the column efficiency is not less than 5000 theoretical plates, 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 $C_{11}H_{20}N_2O_2$ in the injection.

Storage. Store at a temperature not exceeding 30°.