Levetiracetam 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.	

Levetiracetam Injection

Levetiracetam Injection is a sterile solution of levetiracetam in water for Injections. It may contain buffering and isotonicity agents but no antimicrobial agent.

Levetiracetam Injection contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of levetiracetam, $C_8H_{14}N_2O_2$.

Usual strength. 100 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 reference solution (a).

Tests

pH (2.4.24). 5.0 to 6.0.

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. 6 volumes of *acetonitrile* and 94 volumes of *water.*

Test solution. Dilute 2.0 ml of the injection to 200.0 ml with the solvent mixture. Dilute 5.0 ml of the solution to 50.0 ml with the solvent mixture.

Reference solution (a). A 0.01 per cent w/v solution of *levetiracetam IPRS* in the solvent mixture.

Reference solution (b). Dilute 1.0 ml of reference solution (a) to 100.0 ml with the solvent mixture. Further dilute 1.0 ml of the solution to 10.0 ml with the solvent mixture.

Reference solution (c). Dissolve 20 mg of *levetiracetam IPRS* in 10 ml of *0.1 M potassium hydroxide.* Keep the mixture at room temperature for about 15 minutes, then neutralize by adding 10 ml of *0.1 M hydrochloric acid* and dilute to 100.0 ml with the solvent mixture (Solution contains levetiracetam and levetiracetam acid).

Chromatographic system

– a stainless steel column 30 cm x 3.9 mm packed with octadecylsilane bonded to porous silica (10 µm) (Such as MicroBondapak C18),
– mobile phase: a mixture of 60 volumes of *acetonitrile* and 940 volumes of a buffer solution prepared by dissolving 1.0 g of *dipotassium dihydrogen orthophosphate anhydrous* in 1000 ml of *water,* adjusted to pH 6.0 with *orthophosphoric acid,*
– flow rate: 1 ml per minute,
– spectrophotometer set at 205 nm,
– injection volume: 20 µl.

Name	Relative retention time
Levetiracetam acid[1]	0.4
Levetiracetam	1.0

[1](S)-2-(2-Oxopyrrolidin-1-yl)butanoic acid.

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

Inject reference solution (b) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to levetiracetam acid is not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.3 per cent), the area of any secondary peak is not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent) and the sum of the areas of all the secondary peaks is not more than 10 times the area of the principal peak in the chromatogram obtained with reference solution (b) (1.0 per cent).

Bacterial endotoxins (2.2.3). Not more than 0.175 Endotoxin Units per mg of levetiracetam.

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

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

Inject reference solution (a) and (c). The test is not valid unless the tailing factor is not more than 2.0 for levetiracetam peak in the chromatogram obtained with reference solution (c), the relative standard deviation for replicate injections is not more than 1.5 per cent in the chromatogram obtained with reference solution (a).

Inject reference solution (a) and the test solution.

Calculate the content of $C_8H_{14}N_2O_2$ in the injection.

Storage. Store in well closed Type 1 glass vials, at a temperature not exceeding 30°.

Labelling. The label states that the injection is to be diluted prior to administration.