Government of Nepal
Ministry of Health and Population
Department of Drug Administration
National Medicines Laboratory
Quality and Method Validation Section

Analytical profile of Tolvaptan Tablets

Analytical Profile No.: Tolvap 080/81/AP 149

Tolvaptan Tablets contains not less than 90.0% and not more than 110.0% of the stated amount of Tolvaptan.

Usual Strength: 15 mg (Film coated form)

1. Identification:

In the Assay, the principle peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with the certified reference solution.

2. Dissolution: *Determine by liquid chromatography*

2.1 Dissolution Parameters:

Apparatus: Paddle

Medium: 900 ml 0.22% w/v Sodium Lauryl Sulphate.

Speed: 50 rpm

Time: 45 minutes

Withdraw a suitable volume of the medium and filter.

2.3 Test Solution: Use the filtrate.

2.4 Reference Solution: Weigh accurately 20 mg of Tolvaptan WS and transfer in 50 ml completely dried volumetric flask and dissolve in about 30 ml of Solvent mixture. Allow to cool to room temperature. Dilute 1 ml of the solution to 25 ml with dissolution medium.

2.5 Procedure: Use the chromatographic system as described in the Assay using 10 µl as injection volume. Inject the reference solution and the test solution.

Calculate the percent release of Tolvaptan.

2.6 Limit: NLT 70 % of stated amount.

3. Uniformity of Content

Determine by liquid chromatography, as described in the Assay, using the following test solution.

3.1 Test Solution: Take individually 10 tablets and transfer each tablet to 50 ml volumetric flask, disperse in 30 ml of solvent mixture with the aid of sonication. Allow to cool to room temperature and dilute to volume with solvent mixture. Dilute 3 ml of the solution to 10 ml with solvent mixture.

3.2 Reference Solution: Same as assay.

3.3 Limit: NLT 85.0% and NMT 115% of the obtained average content Tolvaptan

4. Assay: *Determine by liquid chromatography*

4.1 Test solution: Weigh 20 tablets and calculate average weight. Weight and dissolve accurately about 50 mg of Tolvaptan in 50 ml of dry volumetric flask, add 30 ml of solvent mixture and dissolve with aid of sonication. Cool to room temperature and dilute to volume with solvent mixture. Further dilute 5 ml of the solution to 20 ml with solvent mixture.

4.2 Reference solution: Weigh accurately 20 mg of Tolvaptan WS and transfer in 50 ml completely dried volumetric flask, add 30 ml of solvent mixture and dissolve with aid of sonication. Cool to room temperature and make up the volume with solvent mixture. Further dilute 5 ml of the solution to 50 ml with solvent mixture.

4.3 Chromatographic system:

Column: C18 (4.6mmX 150-mm, 5µ)

Flow rate: 1.0 ml/min

Wavelength: 260 nm

Injection volume: 20 µl

Column Temperature: 30ºC

Solvent Mixture: 50 volumes of Solution A and 50 volumes of Acetonitrile

Mobile Phase: A mixture of 57 volumes of Solution A and 43 volumes of mixture of 95 volumes of acetonitrile and 5 volumes of water.

Solution A: A mixture of 95 volumes of buffer prepared by dissolve in 1.36 gm. of potassium dihydrogen phosphate into 1000 ml of water, adjust the pH to 3.0 with orthophosphoric acid and 5 volumes of acetonitrile.

4.4 Procedure: Inject the reference solution five times and sample solutions. The test is not valid unless the column efficiency is not less than 2000 theoretical plates, tailing factor is not more than 2.0, and the

relative standard deviation for replicate injections is not more than 2.0%. Measure the peak responses. Calculate the content of Tolvaptan in Tolvaptan Tablets.

5. Other tests: As per Pharmacopoeial requirements.