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

Analytical profile of Telmisartan and Chlorthalidone Tablets

Analytical Profile No.: Telmi Chlor 075/076/AP053

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

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 reference solution.

2. Dissolution Test: *Determine by liquid chromatography*

2.1 Dissolution Parameters:

Apparatus: Paddle

Medium: 900 ml of Phosphate Buffer pH **7.5** (Dissolve 95.2g of potassium dihydrogen orthophosphate and 20.0g of sodium hydroxide in 7000ml of water. Adjust pH 7.5 with 0.1M sodium hydroxide solution.)

Speed and Time: 75 rpm and 45minutes

Withdraw a suitable volume of the medium and filter.

2.2 Test Solution: Use the filtrate.

2.3 Reference Solution A: Weigh accurately 17.5mg of Chlorthalidone WS and transfer into 50 ml dry volumetric flask, add 10 ml of methanol and sonicate for 5 minutes to dissolve drug completely, allow to cool at room temperature and add 30ml dissolution medium, sonicate for 5 minutes and make up the volume with dissolution medium and mix.

2.4 Reference Solution B: Weigh accurately 22.5mg of Telmisartan WS and transfer into 100 ml dry volumetric flask, add 10 ml of methanol and 1ml of 0.1M NaOH, sonicate for 5 minutes to dissolve drug completely, allow to cool at room temperature and add 10ml of **Reference solution A** and make up the volume with dissolution medium and mix. Pipette out 5ml of above solution into 25ml volumetric flask and make up the volume 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 Telmisartan and Chlorthalidone.

2.6 Limit: Not less than 70% (Q) of the stated amount.

3. Uniformity of content (Chlorthalidone):

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

3.1 Test Solution: Weigh 10 tablets individually and place one tablet individually in 100 ml volumetric flask, add about 70 ml of diluents, sonicate for about 15 minutes. Cool at room temperature and make up the volume to mark with same solvents. Dilute 5 of this solution to 50 ml with mobile phase.

3.2 Reference Solution: Weight about 10 mg of Chlorthalidone WS in 100 ml volumetric flask, add about 70 ml of diluents and sonicate for about 5 minutes. Cool at room temperature and make up the volume to mark with same solvents. Dilute 4ml of this solution to 50 ml with mobile phase.

4. Assay: *Determine by liquid chromatography*

4.1 Diluent: Methanol

4.2 Sample Preparation: Weigh individually 20 tablets and calculate average weight. Weigh and transfer 5 tablets into 100ml volumetric flask, add 70ml of diluents, sonicate for 15 minutes with intermittent shaking, cool the solution to room temperature and make up the volume with diluents. Dilute 2 ml of this solution to 100 ml with mobile phase.

4.3 Chlorthalidone Reference Solution: Weigh accurately 10 mg of Chlorthalidone WS and transfer into 100 ml volumetric flask, add 70 ml of diluents and sonicate for 5 minutes, cool to room temperature and make up the volume to 100 ml with same solvent.

4.4 Telmisartan Reference Solution: Weigh accurately 10 mg of Telmisartan WS and transfer into 50 ml volumetric flask, add 30 ml of diluents and sonicate for 5 minutes, cool to room temperature and make up the volume to 50 ml with same solvent.

4.5 Combined Reference Solution: Pipette 4ml of Chlorthalidone reference solution & 10ml of Telmisartan reference solution into 50ml volumetric flask and make up the volume with mobile phase.

4.6 Chromatographic Condition:

Column: Hypersil BDS C18, 250x4.6mm, 5micron or equivalent

Flow rate: 1.0 ml/min

Injection volume: 20µl

Wavelength: 230 nm

Temperature: 30˚C

Mobile Phase: A mixture of 50 volume of Buffer & 50 Volume of Acetonitrile

Buffer: Weigh and dissolve about 7.8 g of sodium dihydrogen orthophosphate dihydrate in 1000ml of water.

4.7 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% and resolution between Chlorthalidone & Telmisartan peak should not be less than 2.0. Measure the peak responses. Calculate the content of Chlorthalidone & Telmisartan in Chlorthalidone & Telmisartan Tablets.

5. Other tests: As per pharmacopoeial requirements.