DEPARTMENT OF DRUG ADMINISTRATION

National Medicines Laboratory

ANALYTICAL METHOD VALIDATION COMMITTEE

Telmisartan and Chlorthalidone Tablets

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

Telmisartan and Chlorthalidone Tablets contains not less than 90 % and not more than 110 % of the stated amount of Telmisartan and Chlorthalidone.

1. Identification:

1.1 Chlorthalidone: In the assay, the principle peak in the chromatogram obtained with the test solution should correspond to the peak in the chromatogram obtained with the reference solution of Chlorthalidone.

1.2 Telmisartan: 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 of Telmisartan.

Tests:

2. Dissolution Test: *Determine by liquid chromatography*

2.1 Dissolution Parameter:

Apparatus:	Paddle
Medium:	900 ml phosphate buffer pH 7.5
Speed and time:	75 rpm for 45min
Temperature:	37˚C ± 0.5˚C

Withdraw a suitable volume of the medium and filter.

2.2 Test Solution: Filter the resulting solution through 0.2 micron filter paper. Use the filtrate.

2.3 Reference Solution:

2.3.1 Reference Solution A: Weigh accurately 17.5 mg of Chlorthalidone reference standard 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 30 ml dissolution medium, sonicate for 5 minutes and make up the volume with dissolution medium and mix.

2.3.2 Mix Reference Solution: Weigh accurately 22.5 mg of Telmisartan reference standard and transfer into 100 ml dry volumetric flask, add 10 ml of methanol and 1 ml of 0.1 M NaOH, sonicate for 5 minutes to dissolve drug completely, allow to cool at room temperature and add 10 ml of Reference **Solution A** and make up the volume with dissolution medium and mix. Pipette out 5 ml of above solution into 25 ml volumetric flask and make up the volume with dissolution medium. Filter through 0.2 micron filter paper.

2.4 Chromatographic Condition and Procedure: Proceed as directed under the Assay using 10 µL injection volume.

Calculate the % release of Telmisartan and Chlorthalidone.

2.5 Limit: Not less than 70 % (D) of the stated amount of Telmisartan and Chlorthalidone.

3. Uniformity of content (Chlorthalidone)**:** *Determine by liquid chromatography*

3.1 Test preparation: Weigh 10 tablets individually and place one tablet individually in 100 ml volumetric flask, add about 70 ml of methanol, sonicate for about 15 minutes. Cool at room temperature and make up the volume to mark with same solvent. Dilute 5 of this solution to 50 ml with mobile phase. Filter the solution through 0.2 µm membrane filter paper.

3.2 Reference Solution: Weight about 10 mg of Chlorthalidone reference standard in 100 ml volumetric flask, add about 70 ml methanol and sonicate for about 5 minutes. Cool at room temperature and make up the volume to mark with same solvent. Dilute 4 ml of this solution to 50 ml with mobile phase and filter the solution through 0.2 µm membrane filter paper.

3.3 Chromatographic Condition: Proceed as directed under the Assay using above mentioned test and reference solution.

Measure the peak response and calculate the content of Chlorthalidone per tablet.

3.4 Limit: 85 – 115 % of the stated amount.

4. Assay: *Determine by liquid chromatography*

4.1 Test Solution: Weigh individually 20 tablets and calculate average weight. Weigh and transfer 5 tablets into 100 ml volumetric flask, add 70 ml methanol, sonicate for 15 minutes with intermittent shaking, cool the solution to room temperature and make up the volume with same. Dilute 2 ml of this solution to 100 ml with mobile phase. Filter the solution through 0.2-micron membrane filter paper.

4.2 Reference Solution:

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

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

4.2.3 Mix Reference Solution: Pipette 4 ml of Chlorthalidone reference solution and 10 ml of Telmisartan reference solution into 50 ml volumetric flask and make up the volume with mobile phase. Filter the final solution through 0.2-micron membrane filter paper.

4.3 Chromatographic Condition:

Column:	C18, 250 x 4.6 mm, 5 micron
Flow rate:	1.0 ml/min
Wavelength:	230 nm
Injection volume:	20 µl
Column Temperature:	30 ˚C
Detector:	UV
Mobile Phase:	Buffer: Acetonitrile (50:50)

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

4.4 Procedure: Inject 20 µl of mix reference solution as per above mentioned chromatographic condition. In the chromatogram obtained from the reference preparation, the column efficiency determined from the major peak should not be less than 2000 theoretical plates, the tailing factor should be not more than 2.0, the relative standard deviation of replicate injections should not be more than 2.0 % and resolution between Chlorthalidone & Telmisartan peak should not be less than 2.0. Calculate the content of Telmisartan and Chlorthalidone in each tablet.

5. Other tests: As per pharmacopoieal requirement.