DEPARTMENT OF DRUG ADMINISTRATION
National Medicines Laboratory
ANALYTICAL METHOD VALIDATION COMMITTEE

Amlodipine & Ramipril Tablets

Analytical Profile No.: Amlo Rami 076/077/AP063

Amlodipine & Ramipril Tablets contain not less than 95 % and not more than 105 % of the stated amount of Amlodipine & Ramipril.

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: Determine by liquid chromatography

2.1 Dissolution Parameter

- **Apparatus:** Paddle
- **Medium:** 900 ml of 0.1N HCl
- **Speed and Time:** 75 rpm & 45 minutes
- **Temperature:** 37+/-0.5°C

2.2 Solvent Mixture: 0.1N HCl:Methanol (20:80)

2.3 Test Solution: Withdraw a suitable volume of the medium and filter. Use the filtrate.

2.4 Reference Solution (a):

Accurately weigh and transfer about 28 mg of Ramipril WS into 100 ml volumetric flask, add about 70ml of solvent mixture, sonicate to dissolve and dilute to volume with solvent mixture and mix well.

Reference Solution (b):

Accurately weigh and transfer about 31 mg of Amlodipine Besylate WS into 100 ml volumetric flask, add about 70ml of solvent mixture, sonicate to dissolve and dilute to volume with solvent mixture and mix well.

Reference Solution (c):

Pipette out 2ml of Reference Solution (a) and 5ml of Reference Solution (b) into a 200 ml volumetric flask and dilute to volume with solvent mixture and mix well.

2.5 Chromatographic System:

Use the chromatographic system as described in the Assay.

2.6 Procedure:

Inject the reference solution and the test solution. The test is not valid unless the column efficiency is not less than 2000 theoretical plates, the tailing factor is not more than 2.0, the relative standard deviation for replicate injections in not more than 2.0% and the resolution between Ramipril and Amlodipine is not less than 2. Calculate the content of Ramipril and Amlodipine**.**

2.7 Limit:

D. Not less than 75% of the stated amount

3. Assay: Determine by Liquid Chromatography

3.1 Solvent Mixture: 0.1N HCl:Methanol (20:80)

3.2 Test Solution:

Determine the average weight of 20 tablets. Transfer 10 tablets into 250ml volumetric flask, add about 170 ml of solvent mixture, shake gently to disperse, sonicate for about 20 minutes with intermediate shaking, cool and make up the volume to the mark with solvent mixture. Centrifuge the solution at 3000 rpm for 10 minutes.

3.3 Reference Solution (a):

Accurately weigh and transfer about 25 mg of *Ramipril WS* into 50 ml volumetric flask, add about 35ml of solvent mixture, sonicate to dissolve and dilute to volume with solvent mixture and mix well.

Reference Solution (b):

Accurately weigh and transfer about 70 mg of *Amlodipine Besylate WS* into 50 ml volumetric flask, add about 35ml of solvent mixture, sonicate to dissolve and dilute to volume with solvent mixture and mix well.

Reference Solution (c):

Pipette out 10 ml of Reference Solution (a) and 10 ml of Reference Solution (b) into a 50 ml volumetric flask and dilute to volume with solvent mixture and mix well.

3.4 Chromatographic system:

- **Column:** C18, (250 x 4.6 mm), 5 µm
- **Flow rate:** 1.5 ml/min
- **Wavelength:** 210 nm
- **Injection volume:** 5 µl
- **Column Temperature:** 50ºC

- **Detector:** UV

Mobile phase: A mixture of 60 volumes of buffer and 40 volumes of Acetonitrile.

Buffer solution: prepared by dissolving 5.0 g of Sodium perchlorate monohydrate in 1000 ml of HPLC water, and adjusting pH to 2.5 with orthophosphoric acid.

3.5 Procedure:

Inject the reference solution and the test solution. The test is not valid unless the column efficiency is not less than 2000 theoretical plates, the tailing factor is not more than 2.0, the relative standard deviation for replicate injections in not more than 2.0% and the resolution between Ramipril and Amlodipine is not less than 2. Calculate the content of Ramipril and Amlodipine in the tablets.

4. Uniformity of Content:

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

4.1 Test solution: Weigh 10 tablets and transfer each into 50 ml volumetric flask. Add about 35ml of solvent mixture shake to disperse, sonicate for about 20 minutes; cool and make up the volume to the mark with solvent mixture. Centrifuge the solution at 3000 rpm for 10 minutes.

4.2 Chromatographic System: Use the chromatographic system as described in the Assay.

4.3 Procedure: Proceed the process as described in assay method. Calculate the content of Ramipril and Amlodipine in the tablets.

4.4 Limit: 85%-115% of the stated amount

5. Other tests: As per pharmacopoeial requirement.