DEPARTMENT OF DRUG ADMINISTRATION

National Medicines Laboratory

ANALYTICAL METHOD VALIDATION COMMITTEE

Metformin (Immediate Release) & Glimepiride Tablets

Analytical Profile No: Met Gli 073/074/AP 015

Metformin (Immediate Release) & Glimepiride Tablets contain not less than 90% and not more than 110% of the stated amount of Metformin and Glimepiride.

1. Identification:

1.1. Metformin HCl:

In the assay, the principle peak in the chromatogram obtained with the sample solution should correspond to the peak in the chromatogram obtained with the reference standard solution of Metformin HCl.

1.2. Glimepiride:

In the assay, the principle peak in the chromatogram obtained with the sample solution corresponds to the peak in the chromatogram obtained with the reference standard solution of Glimepiride.

2. Dissolution:

2.1 Metformin: Determine by UV Spectroscopy

2.1.1 Dissolution Parameters:

- **Apparatus:** Basket
- **Medium:** 900 ml of a 0.68 % w/v solution of potassium dihydrogen orthophosphate, of pH 6.8
- **Speed and Time:** 100 rpm & 45 minutes

Withdraw a suitable volume of the medium and filter

2.1.2 Test Solution: Use the filtrate.

2.1.3 Reference Solution:

Weigh accurately about 25 mg of working standard of metformin hydrochloride and transfer into 100 ml volumetric flask. Dissolve with dissolution medium and make up the volume to 100 ml with dissolution medium. Dilute 2 ml of the standard solution to 100 ml with dissolution medium.

2.1.4 Procedure: Dilute 2 ml of the filtrate to 100 ml with dissolution medium. Measure the absorbance of the standard and sample solution at about 232 nm.

Calculate the percentage of drug release in the tablet.

2.1.5 Limit:

D. Not less than 70 % of the stated amount

2.2 Glimepiride: Determine by liquid chromatography

2.2.1 Dissolution Parameters:

- **Apparatus:** Paddle
- **Medium:** 900 ml of phosphate buffer pH 7.8
- **Speed and Time:** 75 rpm & 30 minutes
- **Temperature:** 37 ± 0.5 °C

Withdraw a suitable volume of the medium and filter

2.2.2 Diluent: 90 % ACN & Dissolution medium

2.2.3 Test Solution: Use the filtrate.

2.2.4 Reference Solution:

Weigh accurately about 22 mg of working standard of Glimepiride and transfer into 100 ml volumetric flask. Add 70 ml of diluent and sonicate for 5 minutes. Cool to room temperature and make up the volume to 100 ml with diluent. Dilute 1 ml of the resulting solution to 200 with dissolution medium. Filter the resulting standard solution.

2.2.5 Chromatographic system

Determine by liquid chromatography, as described in the Assay

2.2.6 Procedure: Separately inject 20 µl of standard and sample solution and blank solution (dissolution medium) and obtain the respective chromatograms. Measure the peak responses. Calculate the % release of the drug.

2.2.7 Limit:

D. Not less than 75 % of the stated amount

3. Uniformity of Content (Glimepiride):

3.1 Test Solution:

Select not fewer than 10 tablets. Weigh individually 10 tablets and transfer individually into ten 100 ml volumetric flask. Add about 75 ml of diluent and sonicate for 30 minutes with intermittent shaking. Allow the sample to cool to room temperature and make up the volume to 100 ml with diluent. Centrifuge the resulting solution and filter the final solution through 0.2 µm membrane filter.

3.2 Reference Solution:

Weigh accurately about 25 mg of metformin hydrochloride and 25 mg of Glimepiride working standard and transfer into 100 ml volumetric flask. Add about 70 ml of the diluent and dissolve with the aid of sonicator and make up the volume to 100 ml with diluent. Dilute 2 ml of the resulting solution to 50 ml with diluent. Filter the final standard solution through 0.2 µm membrane filter.

3.3 Chromatographic Condition:

Same as Assay method

3.4 Procedure:

Inject 20 µl of standard and sample solution separately and obtain the respective chromatogram. Measure the peak responses.

3.5 Limit:

85-115 % of the stated amount of Glimepiride

4. Assay: Determine by liquid chromatography

4.1 Test Solution

4.1.1 Metformin Test solution:

Weigh 20 tablets individually and crush the tablet in the fine powder. Weigh accurately the powder equivalent to 50 mg of metformin and transfer into 100 ml volumetric flask. Add about 70 ml of the diluent and dissolve with the aid of sonicator and make up the volume to 100 ml with diluent. Centrifuge the resulting solution and dilute 2 ml of the resulting solution to 100 ml with diluent. Filter the final standard solution through 0.2 µm membrane filter.

4.1.2 Glimepiride Test solution:

Weigh accurately the powder equivalent to 1 mg of glimepiride and transfer into 100 ml volumetric flask. Add about 70 ml of the diluent and dissolve with the aid of sonicator and make up the volume to 100 ml with diluent. Centrifuge the resulting solution and filter the solution through 0.2 µm membrane filter.

4.2 Reference Solution:

Weigh accurately about 25 mg of metformin hydrochloride and 25 mg of Glimepiride working standard and transfer into 100 ml volumetric flask. Add about 70 ml of the diluent and dissolve with the aid of sonicator and make up the volume to 100 ml with diluent. Dilute 2 ml of the resulting solution to 50 ml with diluent. Filter the final standard solution through 0.2 µm membrane filter.

4.3 Chromatographic system

- **Column:** C 18 (4.6 X 250 cm), 5um

- **Flow rate:** 1.0 ml/min
- **Wave length:** 228 nm
- **Injection volume:** 20 µl
- **Column temperature:** 25 ºC
- **Detector:** UV Detector

Mobile Phase: Buffer : Acetonitrile : Tetrahydrofuran (40 : 50 : 10)

Buffer: Dissolve 7.1 g of dipotassium hydrogen orthophosphate in 1000 ml of HPLC water. Adjust pH to 5.0 with orthophosphoric acid.

Diluent: 90 % ACN

4.4 Procedure:

Separately inject 20 µl of standard and sample solution and obtain the respective chromatograms. Measure the peak responses. Inject the five replicate standard solutions for the system suitability test parameter. The first major peak will be Metformin Hydrochloride and second peak will be Glimepiride. Calculate the content of Metformin and Glimepiride in the tablets.

5. Other tests: As per pharmacopoeial requirement.