DEPARTMENT OF DRUG ADMINISTRATION
National Medicines Laboratory
ANALYTICAL METHOD VALIDATION COMMITTEE

Metformin (Immediate Release) & Linagliptin Tablets

Analytical Profile No.: LMI 074/075/AP 030

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

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. Linagliptin:

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 Linagliptin.

2. Dissolution: Determine by thin layer chromatography and UV spectroscopy

2.1 Dissolution Parameters:

Apparatus: Paddle

Medium: 900 ml, 0.1NHCl

Speed and Time: 50rpm for 45min

Temperature: 37+/-0.5℃

2.2 Chromatographic Condition (Linagliptin):

Column: C18, 150*4.6 mm, 5 µm

Flow rate: 1.0 ml/min

Wavelength: 295 nm

Injection volume: 20 µl

Column temperature: 25 °C

Detector: PDA Detector

2.3 Test Solution:

Place 1 tablet in each dissolution vessel and run the apparatus as per above condition and collect the sample solution from each jar at specified time. After the completion of the dissolution, filter the resulting solution.

2.4 Reference Solution:

Linagliptin Reference solution:

Weigh accurately about 12.5 mg Linagliptin working standard in 100 ml volumetric flask and add 70 ml dissolution medium. Dissolve by sonication and diluted to 100 ml with dissolution medium. Dilute 2 ml resulting solution to 100 ml with dissolution medium. Filter the resulting standard solution through 0.2 µm membrane filter. (2.5ppm)

Metformin Hydrochloride Reference solution:

Weigh accurately about 10 mg Metformin Hydrochloride working standard in 50 ml volumetric flask and add 35 ml dissolution medium. Dissolve by sonication and diluted to 50 ml with dissolution medium. Dilute 5 ml resulting solution to 50 ml with dissolution medium. Filter the resulting standard solution through 0.2 µm membrane filter. (20 ppm)

2.5 Procedure:

Linagliptin: Separately inject 20 µl of standard and test solution and blank solution (dissolution medium) and obtain the respective chromatograms. 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.Measure the peak responses and calculate the % release of the drug.

Metformin Hydrochloride:

Dilute 2ml of test solution to 50ml volumetric flask with dissolution medium. Measure the absorbance of the sample and standard solution in UV-Vis spectrophotometer at about 232 nm and calculate the percentage release.

2.6Limit:

Metformin: D. Not less than 70 % of the stated amount

Linagliptin: D. Not less than 80 % of the stated amount

3. Uniformity of content (Linagliptin)

3.1Test Solution:

Weigh10 tablets and transfer individually to 100ml volumetric flask. Add 60ml of mobile phase and sonicate for 15 min to disperse the tablet. Make up the volume with mobile phase. Filter the final solution through 0.2 µm membrane filter (25ppm)

3.2 Reference Solution:

Weigh accurately about 12.5 mg Linagliptin working standard in 50 ml volumetric flask and add 35 ml mobile phase. Dissolve by sonication and diluted to 50 ml with mobile phase. Dilute 5 ml resulting solution to 50 ml with mobile phase. Filter the resulting standard solution through 0.2 µm membrane filter. (25ppm)

3.3 Chromatographic system: Same as Assay

3.4 Procedure:

Inject 20 µl of standard and sample solution separately. 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 % release of Metformin and Linagliptin.

3.5 Limit: 85-115 % of the stated amount

4. Assay: Determine by liquid chromatography

4.1 Chromatographic System:

Column: C18, 150*4.6 mm, 5 µm

Flow rate: 1.0 ml/min

Wavelength: 265 nm (Metformin), 295 nm (Linagliptin)

Injection volume: 20 µl

Column temperature: 25°C

Detector: PDA Detector

Buffer: 0.02M Phosphate buffer

Mobile phase: Buffer: Acetonitrile (70:30)

4.2 Test Solution:

Weigh individually 20 tablets & crush the tablet into fine powder. Weigh accurately the powder eq. to 500 mg of Metformin HCl in 100ml flask, add 70 ml of mobile phase & sonicate for 15minutes to dissolve. After sonication make volume up to mark with mobile phase. Filter the final solution through 0.2 µm membrane filter.

4.3 Reference Solution:

Metformin HCl Reference Solution:

Weigh accurately about 42.5 mg of working standard of Metfornin HCl and transfer into 20 ml volumetric flask and sonicate to dissolve.

Linagliptin Reference Solution:

Weigh accurately about 12.5 mg Linaliptin working standard into separate 100 ml volumetric flask. Add about 70 ml of mobile phase and sonicate for about 10 minutes and make up the volume to 100 ml with mobile phase.

Mix Reference Solution:

Pipette 2 ml of Linagliptin standard solution to 20ml with mobile phase in a volumetric flask of Metformin HCl and make upto mark with mobile phase.

Note: Adjust the concentration of the reference solution and test solution depending upon the strength of Metformin and Linagliptin Tablet.

4.4 Procedure:

Inject 20 µl of standard and sample solution separately. 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. Resolution between two peaks should be not less than 2. Calculate the content of Metformin and Linagliptin per tablet.

5. Other Test: As per pharmacopoieal requirement.