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

Analytical profile of Metformin Immediate Release & Sitagliptin Tablets

Analytical Profile No.: MetI Sit 073/074/AP 021

Metformin Immediate Release & Sitagliptin Tablets contains not less than 90.0% and not more than 110.0% of the stated amount of Metformin hydrochloride & Sitagliptin.

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:

2.1 Dissolution (Sitagliptin): *Determine by liquid chromatography*

2.1.1 Dissolution Parameters:

Apparatus: Basket

Medium: 900 ml of Water

Speed and Time: 100 rpm and 30 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 36.885 mg of Sitagliptin Phosphate Monohydrate RS eq. to 27.75 mg Sitagliptin and dissolve in water to produce 50 ml. Dilute 5 ml to 50 ml with water.

2.1.4 Procedure: Use the chromatographic system as described in the Assay using 20 µl as injection volume. Inject the reference solution and the test solution.

Calculate the percent release of Sitagliptin.

2.1.5 Limit: Not less than 75% (Q) of the stated amount of Sitagliptin.

2.2 Dissolution (Metformin): *Determine by UV-Vis Spectrophotometry*

2.2.1 Dissolution Parameters:

Apparatus: Basket

Medium: 900 ml of phosphate buffer pH 6.8 (27.22 g of monobasic potassium phosphate in 1000 ml water. Take 250 ml of the solution and add 112 ml of 0.2 M sodium hydroxide solution, then dilute to 1000 ml with water. Adjust the pH to 6.8.)

Speed and Time: 100 rpm and 45 minutes

Withdraw a suitable volume of the medium and filter.

2.2.2 Test Solution: Dilute 1 ml of the filtrate to 100 ml with dissolution medium.

2.2.3 Reference Solution: Weigh accurately about 25 mg of Metformin Hydrochloride RS and transfer into 100 ml volumetric flask. Dissolve with water and make up the volume to 100 ml with water. Dilute 2 ml of the solution to 100 ml with dissolution medium.

2.2.4 Procedure: Measure the absorbance of the standard and sample solution at about 232 nm. Calculate the percent release of Metformin Hydrochloride.

2.2.5 Limit: Not less than 70% (Q) of the stated amount of Metformin Hydrochloride.

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

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

3.1 Test Solution: Take a single tablet, crush and transfer to 100 ml volumetric flask with the help of 70 ml diluents. Sonicate for 30 min and diluted to 100 ml with diluents. Filter the solution and dilute 5 ml of filtrate to 50 ml with the diluent. Prepare similarly for 9 more tablets.

3.2 Reference Solution: Weigh accurately about 33 mg of Sitagliptin Phosphate Monohydrate RS eq. to 25 mg Sitagliptin in 50 ml volumetric flask and add 35 ml diluents. Dissolve by sonication and diluted to 50 ml with diluents. Dilute 5 ml resulting solution to 50 ml with diluents.

4. Assay: *Determine by liquid chromatography*

4.1 Diluents: 5 volume of Acetonitrile and 95 volume of 0.1% v/v orthophosphoric acid in water.

4.2 Test Solution: Weigh individually 20 tablets & crush the tablet into fine powder. Weigh accurately the powder eq. to 50 mg of Metformin HCl and transfer to 100 ml flask, add 70 ml of diluents & sonicate for 15 minutes to dissolve. After sonication, dilute to 100 ml with diluents and stir for 20 minutes, filter through filter paper and dilute 5 ml filtrate to 25 ml with diluents.

4.3 Reference Solution (850 mg metformin+ 50 mg Sitagliptin Tablet):

4.3.1 Metformin HCl Reference Solution: Weigh accurately about 25 mg of Metfornin HCl RS and transfer into 50 ml volumetric flask. Add about 35 ml of diluent and sonicate for about 10 minutes and make up the volume to 50 ml with diluents.

4.3.2 Sitagliptin Reference Solution: Weigh accurately about 30 mg eq. of Sitagliptin from Sitagliptin Phosphate RS into separate 100 ml volumetric flask. Add about 70 ml of diluent and sonicate for about 10 minutes and make up the volume to 100 ml with diluents. Dilute 5 ml of Sitagliptin standard solution to 50 ml with diluents.

4.3.3 Combined Reference Solution: Pipette 5 ml of Metformin HCl reference solution & Sitagliptin reference solution into 25 ml volumetric flask and make up the volume to 25 ml with diluent.

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

4.4 Chromatographic system

Column: Octyldecylsilane (C18), (250 x 4.6 mm), 5 µm

Flow rate: 1.0 ml/min

Detector: UV Detector

Wavelength: 205 nm

Injection volume: 20 µl

Oven temperature: 30 °C

Mobile phase: 75 volume of Buffer and 25 volume of Acetonitrile

Buffer: Weigh 1.36 gm KH_2PO_4, dissolve in 900 ml water and add 2.5 ml of triethylamine. Adjust to pH 3.5 with orthophosphate and dilute to 1000 ml with water.

4.5 Procedure: Inject the reference solution five times and test 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%. Measure the peak responses. Calculate the content of Metformin HCl and Sitagliptin.

5. Other tests: As per pharmacopoeial requirements.