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

Analytical profile of Empagliflozin and LinagliptinTablets

Analytical Profile No.: Empa Lina 080/81/AP 157

Empagliflozin and Linagliptin Tablets contains not less than 90.0% and not more than 110.0% of the stated amount of Empagliflozin and Linagliptin.

Usual Strength: Empagliflozin 25 mg and Linagliptin 5 mg

Empagliflozin 10 mg and Linagliptin 5 mg

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 certified reference solution.

2. Dissolution: *Determine by liquid chromatography*

2.1 Dissolution Parameters:

Apparatus: Paddle

Medium: 900 ml of Phosphate Buffer pH 6.8 (Dissolve 6.8 gm. of Potassium Dihydrogen phosphate in water, dilute to 1000 ml with mater and mix. Adjust the pH 6.8 with sodium hydroxide or 0.1M Hydrochloric acid)

Speed and Time: 50 RPM and 45 minutes

Withdraw a suitable volume of the medium and filter.

2.3 Test Solution: Use the filtrate.

2.4 Reference Solution:

Empagliflozin Standard: Weigh about 28.0 mg WS in 100 ml volumetric flask. Dissolve by adding 60 ml of diluent and sonicate for 10 minutes. Cool to room temperature and make up the volume with diluent.

Linagliptin Standard: Weigh about 14.0 mg WS in 100 ml volumetric flask. Dissolve by adding 60 ml diluent and sonicate for 10 minutes. Cool to room temperature and make up the volume with diluent.

Combined standard solution:

(For 25/5 mg combination): Pipette 5 ml of Empagliflozin stock solution and 2 ml of Linagliptin stock solution into 50 ml volumetric flask and make up the volume with dissolution media, Filter the solution through 0.2 membrane filter.

(For 10/5 mg combination): Pipette 2 ml of Empagliflozin stock solution and 2 ml of Linagliptin stock solution into 50 ml volumetric flask and make up the volume with dissolution media, Filter the solution through 0.2 membrane filter.

2.5 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 Empagliflozin and Linagliptin.

2.6 Limit: NLT 75 % (D) of the stated amount of Empagliflozin and NLT 80 % (D) of the stated amount of Linagliptin.

3. Uniformity of Content:

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

3.1 Test Solution: Place one tablet in 100 ml completely dried volumetric flask. Add 60 ml of diluent and sonicate for 15 minutes. Cool to room temperature, dilute with diluent to volume, and mix. Dilute 3 ml of filtrate to 25 ml with mobile phase and filter.

3.2 Reference Solution: Same as assay.

3.3 Limit: NLT 85.0% and NMT 115% of the obtained average content Atorvastatin.

4. Assay: *Determine by liquid chromatography*

4.1 Test solution: Weigh and powder 20 tablets. Weigh accurately the powder equivalent to 15 mg of Linagliptin and transfer into 100 ml of volumetric flask. Add 60 ml of diluent, sonicate for about 10 minutes, cool the solution to room temperature and make up the volume with diluents. Centrifuge or filter the sample through Whatman No.1 filter paper. Dilute 2 ml to 50 ml with mobile phase. Filter the solution through 0.2 m membrane filter.

4.2 Reference solution:

Empagliflozin Standard: Weigh about 30.0 mg WS in 100 ml volumetric flask. Dissolve by adding 60 ml of diluent and sonicate for 10 minutes. Cool to room temperature and make up the volume with diluent.

Linagliptin Standard: Weigh about 15.0 mg WS in 100 ml volumetric flask. Dissolve by adding 60 ml diluent and sonicate for 10 minutes. Cool to room temperature and make up the volume with diluent.

Combined standard solution:

(For 25/5 mg combination): Pipette 5 ml of Empagliflozin stock solution and 2 ml of Linagliptin stock solution into 50 ml volumetric flask and make up the volume with mobile phase, Filter the solution through 0.2 membrane filter.

(For 10/5 mg combination): Pipette 2 ml of Empagliflozin stock solution and 2 ml of Linagliptin stock solution into 50 ml volumetric flask and make up the volume with mobile phase, Filter the solution through 0.2 membrane filter.

4.3 Chromatographic system:

Column: C18 (4.6mmX 150-mm, 5µ)

Flow rate: 1.0 ml/min

Wavelength: 227 nm

Injection volume: 20µl

Column Temperature: 30ºC

Diluent: Acetonitrile: Water: 50:50

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Mobile Phase: A mixture of 70 volumes of Buffer and 30 volumes of Acetonitrile.

Buffer: Dissolve 5.444 gm. of Potassium dihydrogen orthophosphate in 1000 ml water. Adjust pH to 4.0 with dilute orthophosphoric acid.

4.4 Procedure: Inject the reference solution five times and sample 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 injection for each of the peaks is not more than 2.0%. Measure the peak responses. Calculate the content of Empagliflozin and Linagliptin in Empagliflozin and Linagliptin Tablets.

5. Other tests: As per pharmacopoeial requirements.