**DEPARTMENT OF DRUG ADMINISTRATION**
**National Medicines Laboratory**
**ANALYTICAL METHOD VALIDATION COMMITTEE**

# Linagliptin Tablets

**Analytical Profile No.:** Lina 073/074/ AP 012

Linagliptin Tablets contains not less than 90 % and not more than 110 % of the stated amount of Linagliptin.

**1. Identification:**

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 solution of Linagliptin.

**Tests:**

**2. Dissolution:** *Determine by Liquid Chromatography*

**2.1 Dissolution Parameter:**

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|---|---|
| **Apparatus:** | Basket |
| **Medium:** | 900 ml of 0.1 N hydrochloric acid |
| **Speed and time:** | 50 rpm and 45 minutes |
| **Temperature :** | 37˚C ± 0.5˚C |

Withdraw the suitable volume of the medium and filter.

**2.2 Test Solution:** Use the filtrate, dilute if necessary with dissolution medium to obtain a solution having concentration similar to that of reference solution. Filter through 0.2 micron filter paper.

**2.3 Reference Solution:** Weigh accurately about 28 mg of linagliptin RS and transfer into 100 ml volumetric flask. Dissolve and make up the volume to 100 ml with dissolution medium. Pipette 2 ml of this solution and dilute to 20 ml with dissolution medium. Again dilute 2 ml of the resulting solution to 20 ml with dissolution medium. Filter through 0.2 micron filter paper. (2.8 ppm)

**2.4 Chromatographic system:** Proceed as directed under Assay

**2.5 Procedure:** Inject 20 µl of standard preparation using above mentioned chromatographic conditions. 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 in not more than 2.0 %. After the completion of the system suitability test parameter, inject 20 µl of each of the sample solution separately. Calculate the per cent release of drug in the Linagliptin tablet.

**2.6 Limit:** Not less than 80 % (D) of the stated amount.

**3. Uniformity of content:** *Determine by Liquid Chromatography*

**Diluents:** 0.1 N HCl

**3.1 Test Solution:** Weigh 10 tablet individually and transfer into 100 ml volumetric flask. Add about 70 ml of diluent, sonicate for about 10 minutes, cool the solution to room temperature and make up the volume to 100 ml with diluents. Centrifuge the solution, dilute the supernatant liquid to obtain the solution having similar concentration to that of reference solution. Filter the resulting solution through 0.2 micron filter paper.

**3.2 Reference Solution:** Weigh accurately about 30 mg linagliptin RS and transfer into 100 ml volumetric flask. Dissolve in diluent and make up the volume to 100 ml with the same solvent. Pipette 2 ml of this solution and dilute to 20 ml with diluent. Again dilute 2 ml of the resulting solution to 20 ml with diluent. Filter through 0.2 micron filter paper.

**3.3 Chromatographic system and procedure:** Proceed as directed under assay.

**3.4 Limit:** 85 – 115 % of the stated amount.

**4. Assay:** *Determine by Liquid Chromatography*

**Diluents:** 0.1 N HCl

**4.1 Test Solution:** Weigh individually 20 tablets and crush them into fine powder. Weigh accurately the powder equivalent to 10 mg of linagliptin and transfer into 100 ml volumetric flask. Add about 70 ml of diluent, sonicate for about 10 minutes, cool the solution to room

temperature and make up the volume to 100 ml with diluents. Centrifuge the solution, dilute 3 ml of the supernatant liquid to 100 ml with diluent. Filter the solution with 0.22 micron filter paper.

**4.2 Reference Solution:** Weigh accurately about 30 mg linagliptin RS and transfer into 100 ml volumetric flask. Dissolve in 0.1 N HCl and make up the volume to 100 ml with same solvent. Pipette 2 ml of this solution and dilute to 20 ml with 0.1 N HCl. Again dilute 2 ml of the resulting solution to 20 ml with 0.1 N HCl. Filter through 0.2 micron filter paper. (3 ppm)

**4.3 Chromatographic system:**

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| **Column:** | a stainless steel column 25 cm x 4.6 mm, packed with octadecyl silane bonded to porous silica (5 µm), |
| **Flow rate:** | 1.0 ml per minute, |
| **Wavelength:** | 295 nm |
| **Injection volume:** | 20 µl |
| **Detector:** | UV |
| **Column temperature:** | 25˚C |

**Mobile phase:** a mixture of 30 volumes of acetonitrile and 70 volumes of 0.02 M phosphate buffer pH 4.0,

**0.02 M Phospate buffer pH 4.0**: Weigh accurately about 2.7 g of potassium dihydrogen orthophosphate and dilute to 1000 ml with water.

**4.4 Procedure:** Inject 20 µl of standard preparation using above mentioned chromatographic conditions. 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 in not more than 2.0 %. After the completion of the system suitability test parameter, inject 20 µl of each of the sample solution separately.

Calculate the content of Linagliptin in each tablet.

**5. Other tests:** As per pharmacopoeial requirements.