

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

Analytical profile of Cefixime & Clavulanic Acid Tablets

Analytical Profile No.: Cefi Potas 077/078/AP 092

Cefixime & Potassium Clavulanate Tablets contains not less than 90.0% and not more than 120.0% of the stated amount of Cefixime anhydrous and Clavulanic acid.

Usual Strength: Cefixime Trihydrate eq. to Cefixime 200mg & Diluted Potassium Clavulanate eq. to Clavulanic acid 125mg

1. Identification:

In the Assay, the principle peaks in the chromatogram obtained with the test solution corresponds to the peaks in the chromatogram obtained with the reference solution.

Tests:

2. Dissolution:

2.1 Cefixime: *Determine by UV*

2.1.1 Dissolution Parameters:

Apparatus: Basket

Medium: 900ml of 0.05M Potassium Phosphate buffer pH 7.2 prepared by dissolving 47.6 g of Potassium Dihydrogen Orthophosphate in 7000ml water and adjusting pH to 7.2 with 1 M NaOH.

Speed and Time: 100 rpm and 45 minutes

Withdraw a suitable volume of the medium and filter.

Determine by UV-Vis spectroscopy.

2.1.2 Test Solution: Dilute 5 ml of filtrate to 100 ml with dissolution medium.

2.1.3 Reference Solution: Weigh accurately about 55 mg of Cefixime WS in 100 ml volumetric flask. Add 0.5 ml of methanol, mix, add about 75 ml of dissolution medium, sonicate to dissolve. Cool to room temperature and make up the volume to 100 ml with dissolution medium. Further dilute 2 ml of the solution to 100 ml with same solvent.

2.1.4 Procedure: Measure the absorbance of test solution and reference solution at about 288 nm against dissolution medium.

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

[Note: an amount of methanol not to exceed 0.1% of the total volume of the standard solution may be used to bring the reference standard into solution prior to dilution with dissolution medium, and the solution may be sonicated to assure complete dissolution of the reference standard]

Calculate the content of Cefixime.

2.1.5 Limit: Not less than 75 percent (D) of the stated amount of Cefixime.

2.2 Potassium Clavulanate eq. to Clavulanic Acid: *Determine by liquid chromatography*

2.2.1 Dissolution Parameters:

Apparatus: Basket

Medium: 900ml of 0.05M Potassium Phosphate buffer pH 7.2 prepared by dissolving 47.6 g of Potassium Dihydrogen Orthophosphate in 7000ml water and adjusting pH to 7.2 with 1 M NaOH.

Speed and Time: 100 rpm and 45 minutes

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography.

2.2.2 Test Solution: Dilute 5 ml of filtrate to 20 ml with dissolution medium.

2.2.3 Reference Solution: Weigh accurately about 82 mg of diluted Potassium Clavulanate (34 mg Clavulanic acid) WS in 100 ml volumetric flask. Add about 70 ml of mobile phase and sonicate. Cool to room temperature, make up the volume to 100 ml with same solvent, stir for 30 minutes and filter. Further dilute 5 ml of the solution to 50 ml with same solvent.

2.2.4 Procedure: Use the chromatographic system as described in the Assay.

Inject the reference solution and the test solution.

2.2.5 Limit: Not less than 85 percent (D) of the stated amount of Clavulanic acid.

[Note: 119.125mg Potassium Clavulanate eq. to 100mg Clavulanic acid]

3. Assay: *Determine by liquid chromatography*

3.1 Test Solution: Weigh individually 20 tablets & crush the tablet into fine powder. Weigh a quantity of powder equivalent to 50 mg of Cefixime in 100 ml volumetric flask. Add about 70 ml of mobile phase and sonicate to dissolve, cool to room temperature and make up the volume to

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

100 ml with same solvent, stir for 30 min & filter. Filter and dilute 5 ml of filtrate solution to 50 ml with mobile phase.

3.2 Reference Solution: Weigh accurately about 56 mg of Cefixime Trihydrate WS and 75 mg of diluted Potassium Clavulanate WS in 100ml volumetric flask. Add about 70 ml of mobile phase and sonicate to dissolve, cool to room temperature and make up the volume to 100 ml with same solvent, stir for 30 min & filter. Further dilute 5ml of the filtrate solution to 50ml with same solvent. Use this standard preparation within 1 hour of dilution of the solution.

3.3 Chromatographic system:

- **Column:** C18, 25 cm x 4.6 mm, 5 μ m particle size
- **Flow rate:** 1.0 ml/min
- **Wavelength:** 220 nm
- **Injection volume:** 20 μ l
- **Detector:** UV/PDA
- **Column temperature:** 35 °C
- **Mobile Phase:** A mixture of 40 volumes of acetonitrile, 10 volumes of buffer solution and 50 volumes of water. Adjust the pH to 5.0 $\pm$ 0.1 using orthophosphoric acid.

Buffer solution: Dilute 25 ml of Tetrabutylammonium hydroxide solution (10%) with water to obtain 1000 ml of solution.

3.4 Procedure: Inject the reference solution. The test is not valid unless the column efficiency is not less than 2000 theoretical plates, tailing factor is not more than 2.0, the relative standard deviation for replicate injections is not more than 2.0% and resolution between principal peaks is not less than 5.0.

Calculate the content of Cefixime anhydrous and Clavulanic acid in the tablet.

4. Other tests: As per pharmacopoeial requirement.