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

Analytical profile of Sacubitril and Valsartan Tablets

Analytical Profile No.: Sacub Val 080/81/AP 143

Sacubitril and Valsartan Tablets contains not less than 90.0% and not more than 110.0% of the stated amount of Sacubitril and Valsartan.

Usual Strength: 50 mg

Each film coated tablet contains
Sacubitril 24.3 mg
Valsartan 25.7 mg
(As Sodium salt complex)

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)

Speed and Time: 50 RPM and 30 minutes

Withdraw a suitable volume of the medium and filter.

2.3 Test Solution: Use the filtrate.

2.4 Reference Solution: Weigh accurately about 55 mg of (Sacubitril/Valsartan) WS in 100 ml of Volumetric flask. Add about 50 ml of dissolution medium, sonicate to dissolve for 10 minutes and dilute to volume with same medium and mix. Pipette 5 ml of this solution to 50 ml with dissolution medium.

2.5 Procedure: Use the chromatographic system as described in the Assay using 10 µl as injection volume. Inject the reference solution and the test solution.

Calculate the percent release of Sacubitril and Valsartan.

2.6 Limit: Not less than 70 % of the stated amount of Sacubitril and Valsartan.

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3. Assay: *Determine by liquid chromatography*

3.1 Test solution: Crush 20 tablets and weigh accurately powder equivalent to about 50 mg of Sacubitril/Valsartan and transfer into 100 ml volumetric flask. Add about 50 ml of diluents, sonicate to dissolve for 10 minutes, cool to room temperature and dilute to 100 ml with same solvent, mix and filter.

3.2 Reference solution: Weigh accurately about 50 mg of (Sacubitril/Valsartan) working standard and transfer into 100 ml volumetric flask. Add about 50 ml o diluents, sonicate to dissolve for 10 minutes cool to room temperature and dilute to volume 100 ml with the same solvent, mix and filter.

3.3 Chromatographic system:

Column: C18 (4.6mmX 250-mm, 5µ)

Flow rate: 0.8 ml/min

Wavelength: 241 nm

Injection volume: 10µl

Column Temperature: 30ºC

Diluent: Acetonitrile: Water: 50:50

Solvent A: Dissolve 1.36 gm. Of potassium dihydrogen phosphate in 1000 ml water. Adjust the pH of the solution to 3.0 ± 0.05 with dilute orthophosphoric acid.

Solvent B: Methanol

Gradient Programme Given Below:

Time (Minutes)	**Solvent A (v/v)**	**Solvent B (v/v)**
0.01	40	60
5	40	60
15	30	70
20	30	70
26	10	90
30	10	90
35	40	60
45	40	60

3.4 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 corresponding to Valsartan (First peak) and Sacubitril (Second Peak) is not more than 2.0%. Measure the peak responses. Calculate the content of Sacubitril and Valsartan in Sacubitril and Valsartan Tablets.

Note: The first peak is due to

4. Other tests: As per pharmacopoeial requirements.