DEPARTMENT OF DRUG ADMINISTRATION
National Medicines Laboratory
ANALYTICAL METHOD VALIDATION COMMITTEE

RivaroxabanTablets

Analytical Profile No.: Riva 076/077/ AP 077

Rivaroxaban Tablets contain not less than 90 percent and not more than 110 percent of the stated amount of Rivaroxaban.

1. Identification: In the assay, the principle peak in the chromatogram obtained with the test solution should correspond to the peak in the chromatogram obtained with the reference solution of Rivaroxaban.

Tests:

2. Dissolution: *Determine by Liquid Chromatography*

2.1 Dissolution Parameters:

Apparatus: Paddle

Medium: 900 ml of 0.2 % SLS in acetate buffer pH 4.5

Acetate buffer pH 4.5: Dissolve 2.99 g of sodium acetate in 1000 ml water. Adjust pH to 4.5 with acetic acid.

Speed and time: 75 rpm and 45 minutes

Withdraw the suitable volume of the medium and filter.

2.2 Test Solution:

Dilute the filtrate if necessary with dissolution medium. Pass a portion of the solution under test through 0.45 µ nylon filter paper. (0.011 mg/ml)

2.3 Reference Solution:

Weigh accurately about 22.2 mg of Rivaroxaban RS in to a 200 ml clean and dry volumetric flask. Add about 140 ml of mobile phase into the flask, sonicate to dissolve, cool to room temperature and make up the volume to 200 ml with the same solvent. Further dilute 5 ml of the above solution to 50 ml with dissolution media and mix well. Filter the solution through 0.45 µ nylon filter paper. (0.011 mg/ml).

2.4 Chromatographic system and Procedure:

Proceed as directed for the assay.

Calculate the percentage release of Rivaroxaban in each tablet at specified time.

2.5 Limit:

Not less than 75 % (D) of the stated amount of Rivaroxaban.

3. Content Uniformity: *Determine by Liquid Chromatography*

3.1 Test solution:

Transfer individual tablet to a 50 ml volumetric flask, add 30 ml of mobile phase and sonicate for 15 minutes. Cool to room temperature and make up to volume with same and mix well. Dilute if necessary to obtain a solution containing 0.2 mg/ml Rivaroxaban. Filter the final solution through 0.2 µm membrane filter.

3.2 Reference solution:

Proceed as directed under assay.

3.3 Chromatographic system and Procedure:

Proceed as directed under assay. Calculate the content of Rivaroxaban in each tablet.

3.4 Limit: 85 - 115% of the stated amount

4. Assay: *Determine by Liquid Chromatography*

4.1 Test solution:

Weigh individually 20 tablets and crush them to fine powder. Weigh accurately powder equivalent to 20 mg of Rivaroxaban and transfer into 100 ml volumetric flask. Add about 70 ml mobile phase and dissolve by sonicating for about 15-20 minutes. After sonication cool the flask to room temperature and make up the volume to 100 ml with mobile phase. Filter the resulting solution through 0.2 µm membrane filter paper. (0.2 mg/ml)

4.2 Reference solution:

Weigh accurately about 20 mg of Rivaroxaban WS in 100 ml volumetric flask, add 70 ml of mobile phase, mix well by sonicating for about 10 minutes, cool to room temperature and make up the volume to 100 ml using the same solvent. Filter the final solution through 0.2 µm membrane filter. (0.2 mg/ml)

4.3 Chromatographic system:

Column:	C18, (15 cm x 4.6 mm packed with octadecylsilane bonded to porous silica; 5 µm)
Flow rate:	1.0 ml per minute,
Detector:	UV
Wavelength:	250 nm
Injection volume:	10 µl
Column temperature:	30 ^{0}C
Mobile phase:	a mixture of 0.01 M phosphoric acid solution and Acetonitrile (60:40)

4.4 Procedure:

Inject 10 µl of standard preparation five times. The test is not valid unless the column efficiency is not less than 2000 theoretical plates; the 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 10 µl of each of the sample solution separately. Inject blank solution to check any interference and perform bracketing of standard preparation after injecting test solution. Inject the reference solution and the test solution. Calculate the content of Rivaroxaban in each tablet.

5 Other tests: As per pharmacopoeial requirements.