DEPARTMENT OF DRUG ADMINISTRATION
NATIONAL MEDICINES LABORATORY
QUALITY AND METHOD VALIDATION SECTION

Roflumilast Tablets

Analytical Profile No.: Roflumi 078/079/AP 114

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

Usual Strength: 250 mcg

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 reference solution.

Tests:

2. Dissolution: *Deteremine by liquid chromatography*

2.1 Dissolution Parameters:

Apparatus: Paddle

Medium: 1000ml of 1% SLS in phosphate buffer pH 6.8

Speed and Time: 50 rpm and 45 minutes

Withdraw a suitable volume of the medium and filter.

2.2 Phosphate Buffer pH 6.8: Dissolve 6.8 g of Sodium orthophosphate monohydrate in 1000 ml of water and adjust pH 6.8 with NaOH or orthophosphoric acid.

2.2 Test Solution: Use the filtrate.

2.3 Reference Solution: Weigh accurately about 25 mg of Roflumilast WS in 50 ml volumetric flask, dissolve it with methanol by sonication, cool to room temperature and make up the volume with same solvent. Dilute 2 ml of this solution to 200 ml with dissolution medium. Further dilute 1 ml of this solution to 20 ml with dissolution medium.

2.4 Procedure: Use the chromatographic system as described in the Assay. Inject the reference solution and the test solution.

Calculate the percent release of Roflumilast.

2.5 Limit: Not less than 70 percent (D) of the stated amount of Roflumilast.

3. Uniformity of Content

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

Test Solution: Place a tablet in a 100ml volumetric flask, add 70ml of methanol, sonicate to disperse whole tablet with intermittent shaking. Cool, make up the volume to 100 ml with same solvent and mix.

Reference Solution: Dissolve about 25 mg Roflumilast WS with 20 ml methanol by sonication, cool to room temperature and make up the volume to 100 ml with same solvent. Dilute 1 ml of this solution to 100 ml with same solvent.

4. Assay: *Determine by liquid chromatography*

4.1 Test Solution: Weigh and powder 20 tablets. Weigh a quantity of powder equivalent to 5mg of Roflumilast into 100 ml volumetric flask, add about 50 ml of methanol, sonicate, cool and make volume to 100 ml with same solvent.

4.2 Reference Solution: Weigh accurately about 25 mg of Roflumilast WS in 50 ml volumetric flask. Add about 30 ml of methanol, sonicate to dissolve, cool and make volume to 50 ml with same solvent. Dilute 5 ml of this solution to 50 ml with methanol and mix.

4.3 Chromatographic system:

- **Column:** C18, (150 x 4.6 mm), 5 µ particle size
- **Flow rate:** 1.0 ml/min
- **Wavelength:** 245 nm
- **Injection volume:** 10 µl
- **Detector:** UV
- **Mobile Phase:** A mixture of 40 volumes of 0.07% w/v of ammonium acetate in water, 60 volumes of a mixture of 80 volumes of acetonitrile & 20 volumes of methanol.

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 injections is not more than 2.0%. Measure the peak responses. Calculate the content of Roflumilast in the tablets.

5. Other tests: As per pharmacopoeial requirements.