Apremilast Tablets

Apremilast Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of apremilast, $C_{22}H_{24}N_2O_7S$.

Usual strengths. 10 mg ; 20 mg and 30 mg.

Identification

In the Assay, the principal peak in the chromatogram obtained with the test solution corresponds to peak in the chromatogram obtained with the reference solution.

Tests

Dissolution (2.5.2).

Apparatus No. 1,
Medium. 900 ml of phosphate buffer pH 6.8 with 0.5 per cent w/v *sodium lauryl sulphate*,
Speed and time. 75 rpm and 30 minutes.

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14).

Solvent mixture. 95 volumes of *acetonitrile* and 5 volumes of *water*.

Test solution. Use the filtrate and if necessary, dilute with the dissolution medium.

Reference solution. Dissolve a weighed quantity of *apremilast RS* in solvent mixture, and dilute with the dissolution medium to obtain a solution of about the same concentration as the test solution.

Chromatographic system
- a stainless steel column 15 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (3.5 µm),
- mobile phase: a mixture of 50 volumes of *acetonitrile*, 50 volumes of *water* and 1 volume of *triflouroacetic acid*,
- flow rate: 1 ml per minute,
- spectrophotometer set at 230 nm,
- injection volume: 25 µl.

Inject the reference solution. The test is not valid unless the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of $C_{22}H_{24}N_2O_7S$ in the medium.

D. Not less than 70 per cent of the stated amount of $C_{22}H_{24}N_2O_7S$.

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. 5 volumes of *water* and 95 volumes of *acetonitrile*.

Test solution. Disperse a quantity of the powdered tablets containing 20 mg of Apremilast in 5 ml of *water* and add 75 ml of solvent mixture, with the aid of ultrasound for 20 minutes and dilute to 100.0 ml with the solvent mixture, centrifuge and use the clear supernatant liquid.

Reference solution (a). A 0.01 per cent w/v solution of *apremilast RS* in the solvent mixture. Dilute 1.0 ml of the solution to 100.0 ml with the solvent mixture.

Reference solution (b). A solution containing 0.01 per cent w/v of *apremilast impurity B RS* and 0.02 per cent w/v of *apremilast RS* in the solvent mixture.

Chromatographic system
- a stainless steel column 25 cm x 4.6 mm, packed with phenyl group bonded to spherical porous silica (5 µm) (Such as Zorbax SB Phenyl) or equivalent,
- sample temperature: 10º,
- mobile phase: A. a 0.05 per cent v/v solution of *triflouroacetic acid*,
  B. a mixture of 70 volumes of *acetonitrile*, 30 volumes of *methanol* and 0.025 volume of *triflouroacetic acid*,
- a gradient programme using the conditions given below,
- flow rate: 1 ml per minute,
- spectrophotometer set at 230 nm,
- injection volume: 10 µl.

Time (in min)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	95	5
30	10	90
45	10	90
45.1	95	5
50	95	5

Inject reference solutions (a) and (b). The test is not valid unless the resolution between the peaks due to apremilast impurity B and apremilast is not less than 1.5 in the chromatogram obtained with reference solution (b), the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 10.0 per cent in the chromatogram obtained with reference solution (a).

Inject the reference solution (a) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to apremilast impurity B is not more than twice the area of the principal peak in the chromatogram obtained with the reference solution (a) (1.0 per cent), the area of any secondary peak is not more than the area of the principal peak in the chromatogram obtained with the reference solution (a) (0.5 per cent) and the sum of the areas of all the secondary peaks is not more than 4 times the area of the principal peak in the chromatogram obtained with the reference solution (a) (2.0 per cent). Ignore any peak with an area less than 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Uniformity of content. Complies with the test stated under tablets.

Determine by liquid chromatography (2.4.14), as described in the Assay with the following modifications.

Test solution. Disperse one tablet in 10 ml of water, add 150 ml of *acetonitrile*, with the aid of ultrasound for 30 minutes and dilute to 200.0 ml with the *acetonitrile*. Centrifuge and use the supernatant liquid.

Calculate the content of $C_{22}H_{24}N_2O_7S$ in the tablet.

Other tests. Comply with the tests stated under Tablets.

Assay. Determine by liquid chromatography (2.4.14).

Test solution. Weigh and powder 20 tablets. Disperse a quantity of the powder containing 5 mg of Apremilast in 5 ml of *water* and add 75 ml of *acetonitrile* with the aid of ultrasound for 10 minutes and dilute to 100.0 ml with *acetonitrile*, centrifuge and use the clear supernatant liquid.

Reference solution. A 0.005 per cent w/v solution of *apremilast RS* in *acetonitrile*.

Chromatographic system

- a stainless steel column 25 cm x 4.6 mm, packed with phenyl group bonded to spherical porous silica (5 µm) (Such as Zorbax SB Phenyl) or equivalent,
- mobile phase: a mixture of 10 volumes of *water*,10 volumes of *acetonitrile* and 0.01 volume of *triflouroacetic acid*,
- flow rate: 1 ml per minute,
- spectrophotometer set at 230 nm,
- injection volume: 10 µl.

Inject reference solutions. The test is not valid unless the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0 per cent.

Inject reference solution and the test solution.

Calculate the content of $C_{22}H_{24}N_2O_7S$ in the Tablets.

Storage. Store protected from light and moisture, at a temperature not exceeding 30º.