Bosutinib Tablets

Bosutinib Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of bosutinib, $C_{26}H_{29}Cl_2N_5O_3$.

Usual strengths. 100 mg; 400 mg; 500 mg.

CAUTION - Bosutinib is cytotoxic, extra care required to prevent inhaling particles and exposing the skin to it.

Identification

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

Tests

Dissolution (2.5.2).
Apparatus No. 2 (Paddle),
Medium. 900 ml of *0.1M hydrochloric acid,*
Speed and time. 50 rpm and 45 minutes.

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14).

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

Reference solution. Dissolve a quantity of *bosutinib IPRS* in the dissolution medium and dilute with the dissolution medium to obtain a solution containing 0.011 per cent w/v of bosutinib.

Chromatographic system

- a stainless steel column 15 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as Kromasil Eternity XT C-18),
- column temperature: 35º,
- mobile phase: a mixture of 58 volumes of 0.1 per cent v/v of *triethylamine* in *water* and 42 volumes of *acetonitrile,*
- flow rate: 1.5 ml per minute,
- spectrophotometer set at 269 nm,
- injection volume: 10 µl.

Inject the reference solution. The test is not valid unless the column efficiency is not less than 1500 theoretical plates, 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 $C_{26}H_{29}Cl_2N_5O_3$ in the medium.
Q. Not less than 75 per cent of the stated amount of$C_{26}H_{29}Cl_2N_5O_3$.

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. Equal volumes of *acetonitrile* and *water.*

Test solution. Disperse a quantity of the powdered tablets containing 100 mg of Bosutinib in the solvent mixture, with the aid of mechanical shaker for 30 minutes, dilute to 200.0 ml with the solvent mixture, mix and filter.

*Reference solution (a).*A 0.0005 per cent w/v solution of *bosutinib IPRS* in the solvent mixture.

Reference solution (b). Dilute 1.0 ml of reference solution (a) to 20.0 ml with the solvent mixture.

Chromatographic system

- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as YMC Triart),
- column temperature:45º,
- sample temperature: 5º,
- mobile phase: A. a mixture of 95 volumes of a buffer solution prepared by dissolving 3.08 g of *ammonium acetate* in 1000 ml of *water*, adjusted to pH 6.8 with *ammonia solution* and 5 volumes of *acetonitrile,*
  B. a mixture of 90 volumes of *acetonitrile* and10 volumes of *water*,
- a gradient programme using the conditions given below,
- flow rate: 1 ml per minute,
- spectrophotometer set at 265 nm,

- injection volume: 5 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	65	35
25	45	55
33	35	65
40	20	80
45	20	80
45.5	65	35
52	65	35

Inject reference solution (a) and (b). The test is not valid unless the column efficiency is not less than 12000 theoretical plates, the tailing factor is not more than 1.5 and the relative standard deviation for replicate injections is not more than 5.0 per cent in the chromatogram obtained with reference solution (a) and the signal-to-noise ratio is not less than 10 in the chromatogram obtained with reference solution (b).

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

Other tests. Comply with the tests stated under Tablets.

Assay. Determine by liquid chromatography (2.4.14).

Solvent mixture. 70 volumes of *acetonitrile* and 30 volumes of *water.*

Test solution. Weigh and powder 20 tablets. Disperse a quantity of powder containing 250 mg of Bosutinib in the solvent mixture, with the aid of mechanical shaker for 30 minutes and dilute to 250.0 ml with the solvent mixture. Dilute 1.0 ml of the solution to 20.0 ml with the solvent mixture.

Reference solution. A 0.005 per cent w/v solution of *bosutinib IPRS* in the solvent mixture.

Use chromatographic system as described under dissolution.

Inject the reference solution. The test is not valid unless the column efficiency is not less than 1500 theoretical plates, 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 $C_{26}H_{29}Cl_2N_5O_3$ in the tablets.

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