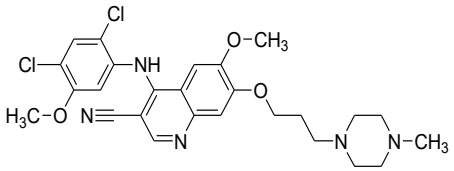
Bosutinib



$C_{26}H_{29}Cl_2N_5O_3$ Mol. Wt. 530.5

Bosutinib is 3-Quinolinecarbonitrile,4-[(2,4-dichloro-5-methoxyphenyl)amino]-6-methoxy-7-[3-(4-methyl-1-piperazinyl)propoxy].

Bosutinib contains not less than 98.0 per cent and not more than 102.0 per cent of $C_{26}H_{29}Cl_2N_5O_3$, calculated on anhydrous basis.

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

Category. Anticancer

Description. A white to yellowish-tan powder.

Identification

A. Determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *Bosutinib IPRS* or with the reference spectrum of bosutinib.

B. 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

Related substances. Determine by liquid chromatography (2.4.14).

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

Test solution. Dissolve 50 mg of the substance under examination in the solvent mixture and dilute to 100.0 ml with the solvent mixture.

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

Reference solution (b). Dilute 5.0 ml of reference solution (a) to 25.0 ml with the solvent mixture.

Chromatographic system

- a stainless steel column 15 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (3 µm) (Such as YMC Triart),
- mobile phase: A. a buffer solution prepared by dissolving 1.74 g of *dipotassium hydrogen orthophosphate* in 1000 ml of *water*, adjusted to pH 10.0 with 1per cent w/v solution of *potassium hydroxide*,
  B. *acetonitrile,*
- a gradient programme using the conditions given below,
- flow rate:1 ml per minute,
- spectrophotometer set at 268 nm,
- injection volume:10 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	75	25
10	35	65
35	35	65
37	75	25
45	75	25

Inject reference solution (a) and (b). The test is not valid unless the column efficiency is not less than 22000 theoretical plates, the tailing factor is not more than 1.5 and the relative standard deviation for replicate injections is not more than 10.0 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 than1.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.3 per cent), the sum of areas of all the secondary peaks is not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (1.0 per cent). Ignore any peak with an area less than 0.25 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Heavy metals (2.3.13). 1.0 g complies with the limit test for heavy metals, Method B (20 ppm).

Sulphated ash (2.3.18). Not more than 0.1 per cent.

Water (2.3.43). Not more than 5.0 per cent, determined on 0.5 g.

Assay. Determine by liquid chromatography (2.4.14).

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

Test solution. Dissolve 50 mg of the substance under examination in the solvent mixture and dilute to 50.0 ml with the solvent mixture. Dilute 5.0 ml of the solution to 100.0 ml with the solvent mixture.

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

Chromatographicsystem

- a stainless steel column 15 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5µm) (Such as X-Bridge C18),
- column temperature: 40º,
- sample temperature:10°,
- mobile phase: a mixture of 50 volumes of 0.1 per cent v/v of *triethylamine* in *water* and 50 volumes of *acetonitrile,*
- flow rate:1 ml per minute,
- spectrophotometer set at 269 nm,
- injection volume:10µl.

Inject the reference solution. The test is not valid unless the column efficiency is not less than 2500 theoretical plates, the tailing factor is not more than 1.5 and the relative standard deviation for replicate injections is not more than 1.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of $C_{26}H_{29}Cl_2N_5O_3$.

Storage. Store protected from moisture, at a temperature not exceeding30º.

Solubility (2.4.26). Soluble in *acetone*; slightly soluble in *ethyl acetate*; insoluble in *water*.