Dasatinib

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Manufacturers, regulatory authorities, health authorities, researchers, and other stakeholders are invited to provide their feedback and comments on this draft proposal. Manufacturers are also invited to submit samples of their products to the IPC to ensure that the proposed monograph adequately controls the quality of the product(s) they manufacture. Comments and samples received after the last date will not be considered by the IPC before finalizing the monograph.

Please send any comments you may have on this draft document to lab.ipc@gov.in, with a copy to Dr. Gaurav Pratap Singh (email: gpsingh.ipc@gov.in) before the last date for comments.

Document History and Schedule for the Adoption Process

Description	Details
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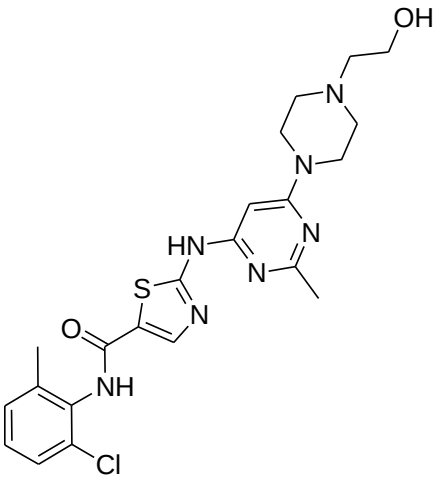
Further follow-up action as required.	

Dasatinib



$C_{22}H_{26}ClN_7O_2S$ Mol. Wt 488.0~~1~~

Dasatinib is N-[2-Chloro-6-methylphenyl]-2-[[6-[4-(2-hydroxyethyl)-1-piperazinyl]-2-methyl-4-pyrimidinyl]amino]-5-thaizolecarboxamide

Dasatinib contains not less than 98.0 per cent and not more than 102.0 per cent of $C_{22}H_{26}ClN_7O_2S$, calculated on anhydrous basis.

Category. Anticancer

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

Description. A white to off-white powder.

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

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).

Test solution. Dissolve 50 mg of the substance under examination in mobile phase B with the aid of ultrasound and dilute to 100.0 ml with mobile phase B.

Reference solution. A 0.005 per cent w/v solution of *dasatinib IPRS* in mobile phase B. Dilute 1.0 ml of the solution to 100.0 ml with mobile phase B.

Chromatographic system

- a stainless steel column 10 cm x 4.6 mm, packed with octadecysilane bonded to porous silica (3µm) (Such as Inertsil ODS-3V C18)
- auto sample temperature: 5°,
- mobile phase: A. a buffer solution prepared by dissolving 0.77 g of *ammonium acetate* in 1000 ml of water,
  B. a mixture of 30 volumes of mobile phase A and 70 volumes of acetonitrile,
- flow rate: 1 ml per minute,
- a gradient programming using the conditions given below,
- spectrophotometer set at 310 nm,
- injection volume: 10 µl.

Time	Mobile phase A	Mobile phase B

(in min.)	(per cent v/v)	(per cent v/v)
0	65	35
3	65	35
35	10	90
40	10	90
40.1	65	35
45	65	35

Name	Relative retention time	~~Relative response~~Correction factor
Dasatinib Impurity A[1]	0.48	-
Dasatinib	1.00	-
Dasatinib Impurity B[2]	1.45	0.82

[1]2-Amino-N-(2-chloro-6-methylpheyl)-thiozole-5-carbomide.
[2]N-(2-chloro-6-methylpheyl)-2-[[6-[1-piperazinyl]-2-methyl-4-pyrimidinyl]amino]-5thiazolecarboxamide.

Inject the reference solution. 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 injection is not more than 5.0 per cent.

Inject the reference solution and test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to dasatinib impurity A and dasatinib impurity B, each of, is not more than 1.5 times the area of the principal peak in the chromatogram obtained with the reference solution (0.15 per cent), the area of any other secondary peak is not more than the area of the principal peak in the chromatogram obtained with the reference solution (0.1 per cent) and the sum of the areas of all the secondary peaks is not more than 10 times the area of the principal peak in the chromatogram obtained with the reference solution (1.0 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.

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

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

Test solution. Dissolve 50 mg of the substance under examination in the solvent mixture with the aid of ultrasound and dilute to 100.0 ml with the solvent mixture. Dilute 1.0 ml of the solution to 20.0 ml with the solvent mixture.

Reference solution. A 0.0025 per cent w/v solution of *dasatinib IPRS* in the solvent mixture.

– Column temperature: 40°C

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	50	50
8	30	70
10	50	50
15	50	50

Inject the reference solution. 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 injection is not more than 2.0 per cent.

Inject the reference solution and test solution.

Calculate the content of $C_{22}H_{26}ClN_7O_2S$.

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

2.4.26 Solubility

Dasatinib. Soluble in Dimethylsulphoxide