Dasatinib Tablets

Published on: …… **Last date for comments:** ……

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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
Document version	3.0
Monograph proposed for inclusion	IP Addendum 2024
Tentative effective date of monograph	April, 2024
First draft published on IPC website for public comments	18 October, 2022
Draft revision published on IPC website for public comments	05 January, 2023 (Version 2.0)
Further follow-up action as required.	

Dasatinib Tablets

Dasatinib Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of dasatinib, $C_{22}H_{26}ClN_7O_2S$.

Usual strengths. 20 mg; 50 mg; 70 mg; 100 mg.

CAUTION- Dasatinib 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. 1000 ml of a buffer solution prepared by dissolving 2.99 g of *sodium acetate trihydrate* in 1000 ml of *water*, adjusted to pH 4.0 with *glacial acetic acid*. Add 10 g of *octoxinol 10*,
Speed and time. 60 rpm and 30 minutes.

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14).

Solvent mixture. 60 volumes of a buffer solution prepared by dissolving 2.72 g of *potassium dihydrogen orthophosphate* in 1000 ml of *water*, adjusted to pH 2.5 with *orthophosphoric acid* and 40 volumes of *methanol*.

Buffer solution. Dissolve 2.72 g of *potassium dihydrogen orthophosphate monohydrate* in 1000 ml of *water*, adjusted to pH 3.0 with *orthophosphoric acid*.

Test solution. Use the filtrate, dilute if necessary, with the solvent mixture.

Reference solution. A 0.001 per cent w/v solution of *dasatinib IPRS* in the solvent mixture.

Chromatographic system
– a stainless steel column 25 cm x 4.6 mm, packed with octadecysilane bonded to porous silica (5µm) (Such as Kromasil),
– column temperature: 30°,
– mobile phase: a mixture of 52 volumes of the buffer solution and 48 volumes of *methanol*,
– flow rate: 1 ml per minute,
– spectrophotometer set at 320 nm,
– injection volume: 50 µl.

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 the test solution.

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

Q. Not less than 75 per cent of the stated amount of $C_{22}H_{26}ClN_7O_2S$.

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. 10 volumes of a buffer solution prepared by dissolving 2.72 g of *potassium dihydrogen orthophosphate* in 1000 ml of *water*, adjusted to pH 2.5 with *orthophosphoric acid* and 90 volumes of *methanol.*

Test solution. Disperse a quantity of powdered tablets containing 100 mg of Dasatinib in the solvent mixture, with the aid of ultrasound for 15 minutes and dilute to 100.0 ml with the solvent mixture, filter.

Reference solution. A 0.0002 per cent w/v solution of *dasatinib IPRS* in the solvent mixture.

Use the chromatographic system as described under Dissolution with the following modifications.
– mobile phase: A. the buffer solution,
B. *methanol*,
– a gradient programme using the conditions given below,

– injection volume: 10 µl.

Time (in min)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	60	40
42	60	40
52	25	75
74	25	75
75	60	40
85	60	40

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 the test solution. In the chromatogram obtained with the test solution, the area of any secondary peak is not more than the area of the principal peak in the chromatogram obtained with the reference solution (0.2 per cent) and 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 (2.0 per cent).

Other tests. Comply with the tests stated in the Tablets.

Assay. Determine by liquid chromatography (2.4.14).

Solvent mixture. 10 volumes of a buffer solution prepared by dissolving 2.72 g of *potassium dihydrogen orthophosphate* in 1000 ml of *water,* adjusted to pH 2.5 with *orthophosphoric acid* and 90 volumes of *methanol.*

Test solution. Weigh and powder 20 tablets. Disperse a quantity of powder containing 100 mg of Dasatinib in the solvent mixture, with the aid of ultrasound for 15 minutes and dilute to 100.0 ml with the solvent mixture. Dilute 1.0 ml of the solution to 10.0 ml with the solvent mixture.

Reference solution. A 0.01 per cent w/v solution of *dasatinib IPRS* in the solvent mixture.

Use the chromatographic system as described under Dissolution with the following modifications.

– injection volume: 10 µl.

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 the test solution.

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

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