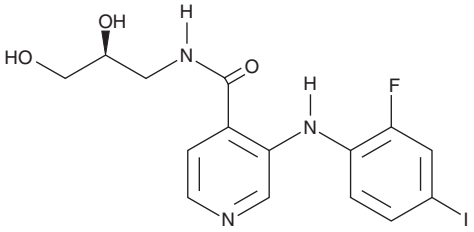
PRODUCT INFORMATION

AS-703026

Item No. 11226

CAS Registry No.: 1236699-92-5
Formal Name: N-[(2S)-2,3-dihydroxypropyl]-3-[(2-fluoro-4-iodophenyl)amino]-4-pyridinecarboxamide
Synonyms: MSC1936369B, Pimasertib
MF: $C_{15}H_{15}FIN_3O_3$
FW: 431.2
Purity: ≥95%
UV/Vis.: λ_{max}: 204, 284, 353 nm
Supplied as: A crystalline solid
Storage: -20°C
Stability: ≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

AS-703026 is supplied as a crystalline solid. A stock solution may be made by dissolving the AS-703026 in the solvent of choice, which should be purged with an inert gas. AS-703026 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of AS-703026 in ethanol is approximately 1 mg/ml and approximately 30 mg/ml in DMSO and DMF.

AS-703026 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, AS-703026 should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. AS-703026 has a solubility of approximately 0.5 mg/ml in a 1:1 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

The mitogen-activated protein kinases, MEK1 and 2, are dual-specificity threonine/tyrosine kinases that play key roles in the activation of the Ras-Raf-MEK-ERK pathway and are often upregulated in a variety of cancer cell types.[1] AS-703026 is an orally bioavailable small molecule that selectively binds to and inhibits MEK1/2, preventing the activation of downstream effector proteins and transcription factors. It potently inhibits growth and survival of human INA-6 multiple myeloma cells and cytokine-induced osteoclast differentiation with IC_{50} values of 10 and 18.2 nM, respectively.[2] In mice bearing H929 MM xenograft tumors, 30 mg/kg AS-703026 reduced tumor growth significantly, which correlated with downregulated ERK1/2 activity, induced PARP cleavage, and decreased microvessels *in vivo*.[2] At 10 µM, AS-703026 supressed proliferation and transformation of K-Ras mutated colorectal cancer cells resistant to EGFR antibody therapy.[3]

References

1. VanScyoc, W.S., Holdgate, G.A., Sullivan, J.E., *et al.* Enzyme kinetics and binding studies on inhibitors of MEK protein kinase. *Biochemistry* (2008).
2. Kim, K., Kong, S.-Y., Fulciniti, M., and *et al.* Blockade of the MEK/ERK signalling cascade by AS703026, a novel selective MEK1/2 inhibitor, induces pleiotropic acnti-myeloma activity *in vitro* and *in vivo*. *Br. J. Haematol.* **149(4)**, 537-549 (2010).
3. Yoon, J., Koo, K.-H., and Choi, K.-Y. MEK1/2 inhibitors AS703026 and AZD6244 may be potential therapies for KRAS mutated colorectal cancer that is resistant to EGFR monoclonal antibody therapy. *Cancer Res.* **71 (445)**, (2011).

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