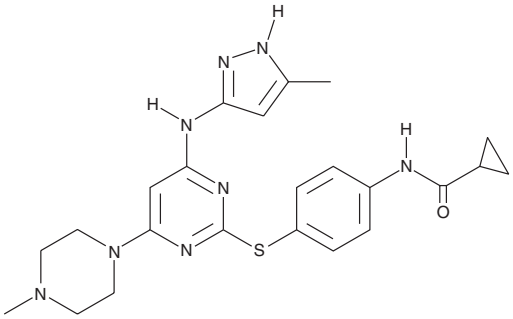
PRODUCT INFORMATION

MK-0457

Item No. 13600

CAS Registry No.: 639089-54-6
Formal Name: N-[4-[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]-cyclopropanecarboxamide
Synonyms: Tozasertib, VX-680
MF: $C_{23}H_{28}N_8OS$
FW: 464.6
Purity: ≥98%
UV/Vis.: λ_{max}: 253 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

MK-0457 is supplied as a crystalline solid. A stock solution may be made by dissolving the MK-0457 in the solvent of choice. MK-0457 is soluble in organic solvents such as DMSO and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of MK-0457 in these solvents is approximately 15 and 20 mg/ml, respectively.

MK-0457 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, MK-0457 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. MK-0457 has a solubility of approximately 0.1 mg/ml in a 1:10 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

The Aurora kinases (A, B, and C) are a family of serine-threonine kinases that regulate various stages of mitotic function. With significant roles in cell cycle and cell division, Aurora kinase gene amplification and overexpression are linked to tumorigenesis.[1] MK-0457 is a potent pan-Aurora kinase inhibitor but favors Aurora A (K_i = 0.6 nM) over Aurora B (K_i = 18 nM) or Aurora C (K_i = 4.6 nM).[2] It shows selectivity against a panel of more than 190 different protein kinases.[2] MK-0457 effectively inhibits proliferation of several different cell lines of clear cell renal carcinoma (IC_{50}s = <10 µM) and blocks the growth of tumors in a rodent model of cancer (80 mg/kg), inhibiting histone H3 phosphorylation and increasing apoptosis.[1] By depleting Aurora activity, MK-0457 disrupts bipolar spindle formation during mitosis, arresting cell cycle progression at the G_2/M phase.[1]

References

1. Li, Y., Zhang, Z.-F., Chen, J., *et al.* VX680/MK-0457, a potent and selective Aurora kinase inhibitor, targets both tumor and endothelial cells in clear cell renal cell carcinoma. *Am. J. Transl. Res.* **2(3)**, 296-308 (2010).
2. Pollard, J.R. and Mortimore, M. Discovery and development of Aurora kinase inhibitors as anticancer agents. *J. Med. Chem.* **52(9)**, 2629-2651 (2009).

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