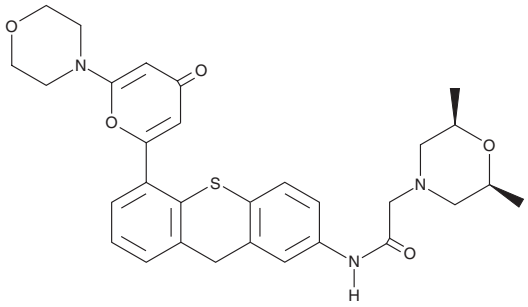
PRODUCT INFORMATION

Ku-60019

Item No. 17502

CAS Registry No.: 925701-46-8
Formal Name: *rel*-2R,6S-dimethyl-N-[5-[6-(4-morpholinyl)-4-oxo-4H-pyran-2-yl]-9H-thioxanthen-2-yl]-4-morpholineacetamide
MF: 547.7
FW: $C_{30}H_{33}N_3O_5S$
Purity: ≥98%
UV/Vis.: λ_{max}: 244, 272 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

Ku-60019 is supplied as a crystalline solid. A stock solution may be made by dissolving the Ku-60019 in the solvent of choice, which should be purged with an inert gas. Ku-60019 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of Ku-60019 in ethanol and DMSO is approximately 50 mg/ml and approximately 20 mg/ml in ethanol and DMF.

Ku-60019 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, Ku-60019 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. Ku-60019 has a solubility of approximately 0.5 mg/ml in a 1:1 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

Ataxia-telangiectasia mutated (ATM) is a serine/threonine kinase that activates checkpoint signaling following double strand DNA breaks and genotoxic stress. Ku-60019 is a potent, reversible inhibitor of ATM kinase (IC_{50} = 6.3 nM), blocking the phosphorylation of ATM substrate proteins.[1,2] It is much less effective or without effect against a panel of 229 other kinases.[1] Ku-60019 sensitizes glioma cells to radiation and inhibits migration and invasion of glioma cells *in vitro*.[1,2] It produces radiosensitization and increases survival *in vivo* when administered intra-tumorally in orthotopic xenograft models of glioblastoma multiforme.[3] Ku-60019 is particularly effective in producing lethality in cells with mutant p53 or that are deficient in PTEN.[3,4]

References

1. Golding, S.E., Rosenberg, E., Valerie, N., *et al.* Improved ATM kinase inhibitor KU-60019 radiosensitizes glioma cells, compromises insulin, AKT and ERK prosurvival signaling, and inhibits migration and invasion. *Mol. Cancer Ther.* **8(10)**, 2894-2902 (2009).
2. Golding, S.E., Rosenberg, E., Adams, B.R., *et al.* Dynamic inhibition of ATM kinase provides a strategy for glioblastoma multiforme radiosensitization and growth control. *Cell Cycle* **11(6)**, 1167-1173 (2012).
3. Biddlestone-Thorpe, L., Sajjad, M., Rosenberg, E., *et al.* ATM kinase inhibition preferentially sensitizes p53-mutant glioma to ionizing radiation. *Clin. Cancer Res.* **19(12)**, 3189-3200 (2013).
4. McCabe, N., Hanna, C.D., Walker, S.M., *et al.* Mechanistic rationale to target PTEN-deficient tumour cells with inhibitors of the DNA damage response kinase ATM. *Cancer Res.* **75(11)**, 2159-2165 (2015).

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