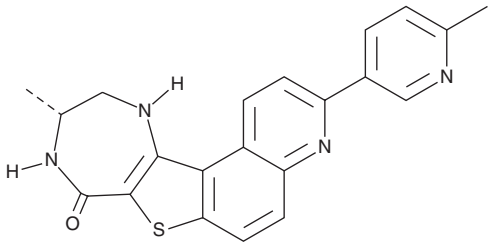
PRODUCT INFORMATION

PF-3644022

Item No. 19185

CAS Registry No.:	1276121-88-0
Formal Name:	(10R)-9,10,11,12-tetrahydro-10-methyl-3-(6-methyl-3-pyridinyl)-8H-[1,4]diazepino[5′,6′:4,5]thieno[3,2-f]quinolin-8-one
MF:	$C_{21}H_{18}N_4OS$
FW:	374.5
Purity:	≥95%
UV/Vis.:	λ_{max}: 255, 287 nm
Supplied as:	A 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

PF-3644022 is supplied as a solid. A stock solution may be made by dissolving the PF-3644022 in the solvent of choice, which should be purged with an inert gas. PF-3644022 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of PF-3644022 in ethanol is approximately 3 mg/ml and approximately 30 mg/ml in DMSO and DMF.

Description

PF-3644022 is an inhibitor of MAPK-activated protein kinase 2 (MK2; IC_{50} = 5.2 nM).[1] It is selective for MK2 over MK3, MAPK-interacting protein kinase 1 (MNK-1), MNK-2, p90 ribosomal S6 kinase 1 (MSK1), MSK2, and p90 ribosomal S6 kinases 1-4 (RSK1-4; IC_{50}s = 53, 3,000, 148, >1,000, >1,000, and >1,000 nM, respectively), as well as a panel of 200 other kinases at 1 µM, but also inhibits MK5/PRAK (IC_{50} = 5 nM). PF-3644022 inhibits LPS-induced TNF-α production in U937 cells and isolated human peripheral blood mononuclear cells (PBMCs) and whole blood (IC_{50}s = 0.159, 0.16, and 1.97 µM, respectively) and reduces paw swelling in a rat model of arthritis induced by streptococcal cell wall peptidoglycan–polysaccharide complexes (ED_{50} = 20 mg/kg). It prevents decreases in motor function in a *twy/twy* mouse model of chronic cervical spinal cord compression when administered at a dose of 30 mg/kg.[2] Peritumoral administration of PF-3644022 (30 µl of a 50 µM solution) enhances radiation-induced decreases in tumor volume and increases in survival in a patient-derived xenograft (PDX) mouse model of head and neck squamous cell carcinoma (HNSCC).[3]

References

1. Mourey, R.J., Burnette, B.L., Brustkern, S.J., *et al.* A benzothiophene inhibitor of mitogen-activated protein kinase-activated protein kinase 2 inhibits tumor necrosis factor α production and has oral anti-inflammatory efficacy in acute and chronic models of inflammation. *J. Pharmacol. Exp. Ther.* **333(3)**, 797-807 (2010).
2. Yu, L., Song, H., Fang, X., *et al.* Role of MK2 signaling pathway mediating microglia/macrophages polarization in chronic compression injury of cervical spinal cord. *Ann. Palliat. Med.* **10(2)**, 1304-1312 (2021).
3. Berggren, K.L., Cruz, S.R., Hixon, M.D., *et al.* MAPKAPK2 (MK2) inhibition mediates radiation-induced inflammatory cytokine production and tumor growth in head and neck squamous cell carcinoma. *Oncogene* **38(48)**, 7329-7341 (2019).

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