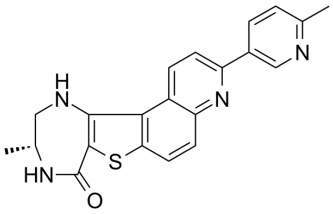
PF-3644022

Cat. No.:	HY-107427
CAS No.:	1276121-88-0
Molecular Formula:	$C_{21}H_{18}N_4OS$
Molecular Weight:	374
Target:	MAPKAPK2 (MK2); p38 MAPK
Pathway:	MAPK/ERK Pathway
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 41.67 mg/mL (111.42 mM; ultrasonic and warming and heat to 80°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.6738 mL	13.3690 mL	26.7380 mL
	5 mM	0.5348 mL	2.6738 mL	5.3476 mL
	10 mM	0.2674 mL	1.3369 mL	2.6738 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (5.56 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

PF-3644022 is a potent, selective, orally active and ATP-competitive MAPKAPK2 (MK2) inhibitor with an IC_{50} of 5.2 nM and a K_i of 3 nM. PF-3644022 also inhibits MK3 and p38 regulated/activated kinase (PRAK) with IC_{50}s of 53 nM and 5.0 nM, respectively. PF-3644022 potently inhibits TNFα production and has anti-inflammatory effect[1].

IC_{50} & Target

IC50: 5.2 nM (MK2), 5.0 nM (PRAK) and 53 nM (MK3)[1].
Ki: 3 nM (MK2)[1]

In Vitro

The inhibitory activity of PF-3644022 against other MAPKAP kinase family members is evaluated. Other than MNK2 with an IC_{50} of 148 nM, other family members are largely not inhibited, showing at least several hundred-fold selectivity versus MK2[1]. In the human U937 monocytic cell line or peripheral blood mononuclear cells, PF-3644022 potently inhibits TNFα production with similar activity (IC_{50} of 160 nM). PF-3644022 blocks TNFα and IL-6 production in LPS-stimulated human whole blood with IC_{50} values of 1.6 and 10.3 μM, respectively. Inhibition of TNFα in U937 cells and blood correlates closely with inhibition

	of phospho-heat shock protein 27, a target biomarker of MK2 activity[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	PF-3644022 (3-100 mg/kg; oral gavage; twice a day; for 12 days; Lewis rats) treatment shows dose-dependent inhibition of chronic paw swelling measured on day 21 after 12 days of oral dosing, with ED_{50} value of 20 mg/kg[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female Lewis rats (125-140 g) injected with streptococcal cell wall[1]
Dosage:	3 mg/kg, 10 mg/kg, 30 mg/kg, 50 mg/kg, 100 mg/kg
Administration:	Oral gavage; twice a day; for 12 days
Result:	Showed dose-dependent inhibition of chronic paw swelling measured on day 21 after 12 days of oral dosing.

REFERENCES

[1]. Mourey RJ, et al. A benzothiophene inhibitor of mitogen-activated protein kinase-activated protein kinase 2 inhibits tumor necrosis factor alpha production and has oral anti-inflammatory efficacy in acute and chronic models of inflammation. J Pharmacol Ex

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA