AMG-548 dihydrochloride

Cat. No.: HY-108642B

CAS No.: 2518299-32-4

Molecular Formula: $C_{29}H_{29}Cl_2N_5O$

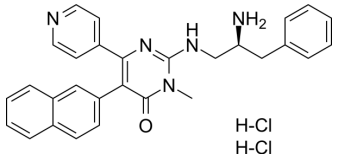
Molecular Weight: 534.48

Target: p38 MAPK; Casein Kinase

Pathway: MAPK/ERK Pathway; Cell Cycle/DNA Damage; Stem Cell/Wnt

Storage: -20°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 10 mg/mL (18.71 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
	1 mM	1.8710 mL	9.3549 mL	18.7098 mL
	5 mM	0.3742 mL	1.8710 mL	3.7420 mL
	10 mM	0.1871 mL	0.9355 mL	1.8710 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1 mg/mL (1.87 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1 mg/mL (1.87 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AMG-548 dihydrochloride, an orally active and selective p38α inhibitor (K_i=0.5 nM), shows slightly selective over p38β (K_i=36 nM) and >1000 fold selective against p38γ and p38δ. AMG-548 dihydrochloride is also extremely potent in the inhibition of whole blood LPS stimulated TNFα (IC_{50}=3 nM)[1]. AMG-548 dihydrochloride inhibits Wnt signaling by directly inhibiting Casein kinase 1 isoforms δ and ε[2].

IC_{50} & Target

p38α 0.5 nM (Ki)	p38β 3.6 nM (Ki)	p38δ 2600 nM (Ki)	p38γ 4100 nM (Ki)
dog p38α 5.0 nM (Ki)	JNK 1 11480 nM (Ki)	JNK 2 39 nM (Ki)	JNK 3 61 nM (Ki)
CK1			

In Vitro	AMG-548 dihydrochloride shows >1000 fold selective against p38γ (K_i=2600 nM) and p38δ (k_i=4100 nM). AMG-548 dihydrochloride has an modest selectivity against JNK2 (k_i=39 nM) and JNK3 (k_i=61 nM). AMG-548 dihydrochloride is also extremely potent in the inhibition of whole blood LPS stimulated TNFa (IC_{50}=3 nM) and IL1b (IC_{50}=7 nM) as well as TNFa induced IL-8 (IC_{50}=0.7 nM) and IL-1b induced IL-6 ($IC50_{50}$=1.3 nM) in human whole blood[1]. AMG-548 dihydrochloride (10 μM) inhibits the hDvl2 shift[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	AMG-548 dihydrochloride has rat F of 62% and dog F of 47%. The $t_{1/2}$ is 4.6 hours in rats and 7.3 hours in dogs[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Lee MR, et al. MAP kinase p38 inhibitors: clinical results and an intimate look at their interactions with p38alphaprotein. Curr Med Chem. 2005;12(25):2979-94.

[2]. Verkaar F, et al. Inhibition of Wnt/β-catenin signaling by p38 MAP kinase inhibitors is explained by cross-reactivity with casein kinase Iδ/ε. Chem Biol. 2011 Apr 22;18(4):485-94.

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