AMG-548 hydrochloride

Cat. No.: HY-108642A

CAS No.: 2437438-16-7

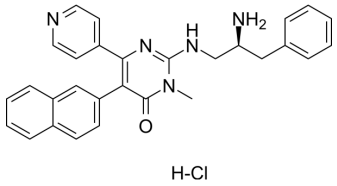
Molecular Formula: $C_{29}H_{28}ClN_5O$

Molecular Weight: 498.02

Target: p38 MAPK; Casein Kinase

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

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	AMG-548 hydrochloride, 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 hydrochloride is also extremely potent in the inhibition of whole blood LPS stimulated TNFα (IC_{50}=3 nM)[1]. AMG-548 hydrochloride 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)	JNK1 11480 nM (Ki)	JNK2 39 nM (Ki)	JNK3 61 nM (Ki)
CK1			

In Vitro

AMG-548 hydrochloride shows >1000 fold selective against p38γ (K_i=2600 nM) and p38δ (k_i=4100 nM). AMG-548 hydrochloride has an modest selectivity against JNK2 (k_i=39 nM) and JNK3 (k_i=61 nM). AMG-548 hydrochloride 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 hydrochloride (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 hydrochloride 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.

Caution: Product has not been fully validated for medical applications. For research use only.

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