TAK-715

Cat. No.: HY-10456

CAS No.: 303162-79-0

Molecular Formula: $C_{24}H_{21}N_3OS$

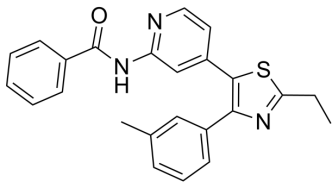
Molecular Weight: 399.51

Target: p38 MAPK; Casein Kinase

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

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (250.31 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.5031 mL	12.5153 mL	25.0307 mL
5 mM	0.5006 mL	2.5031 mL	5.0061 mL
10 mM	0.2503 mL	1.2515 mL	2.5031 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: ≥ 2.5 mg/mL (6.26 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.26 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

TAK-715 is an orally active and potent p38 MAPK inhibitor with IC_{50}s of 7.1 nM, 200 nM for p38α and p38β, respectively. TAK-715 inhibits casein kinase I (CK1δ/ε) to regulate activation of Wnt/β-catenin signaling. TAK-715 shows good significant efficacy in a rat arthritis model[1][2].

IC_{50} & Target

p38α 7.1 nM (IC_{50})	p38β 200 nM (IC_{50})	p38δ >10 μM (IC_{50})	p38γ >10 μM (IC_{50})
CK1δ	CK1ε		

In Vitro

TAK-715 (compound 8h) inhibits LPS-stimulated release of TNF-α from THP-1 (IC_{50}=48 nM) and has no inhibitory activity for major CYPs, including CYP3A4. TAK-715 has no inhibition to p38γ/δ, JNK1, ERK1, IKKβ, MEKK1 or TAK1 (IC_{50}>10 μM of all)[1].
TAK 715 (10 μM; 1 hour) inhibits Wnt-3a-induced hDvl2 phosphorylation and the hDvl2 shift in U2OS-EFC cells[2].
TAK-715 (1 μM; pretreatment for 16 hours) dramatically suppresses Norepinephrine (NE)-stimulated induction of fibronectin, CTGF, and Snai1 expression in TGF-β1-treated HK-2 cells at both the mRNA and protein levels[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

TAK-715 (compound 8h; 3-30 mg/kg; PO) significantly reduces the secondary paw volume[1].
TAK-715 (10 mg/kg; PO) has a C_{max} of 0.19 μg/mL and an AUC of 1.16 μg h/mL.
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	7-week-old male Lewis rats with arthritis[1]
Dosage:	3, 10, 30 mg/kg
Administration:	PO; single dose
Result:	Significantly reduced the secondary paw volume (25% inhibition)

Animal Model:	Rat[1]
Dosage:	10 mg/kg (Pharmacokinetic Analysis)
Administration:	PO
Result:	Had a C_{max} of 0.19 μg/mL and an AUC of 1.16 μg•h/mL.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- J Invest Dermatol. 2019 Jan;139(1):224-234.
- Front Pharmacol. 2018 Jun 21;9:660.
- Drug Des Dev Ther. 2023 Feb 20.
- FASEB J. 2020 Nov;34(11):14892-14904.

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REFERENCES

[1]. Miwatashi S, et al. Novel inhibitor of p38 MAP kinase as an anti-TNF-alpha drug: discovery of N-[4-[2-ethyl-4-(3-methylphenyl)-1,3-thiazol-5-yl]-2-pyridyl]benzamide (TAK-715) as a potent and orally active anti-rheumatoid arthritis agent. J Med Chem, 2005, 48(19), 5966-5979.

[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, 18(4), 485-494.

[3]. Huiwen Ren, et al. Inhibition of α1-adrenoceptor reduces TGF-β1-induced epithelial-to-mesenchymal transition and attenuates UUO-induced renal fibrosis in mice. FASEB J. 2020 Nov;34(11):14892-14904.

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

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