产品名称：TAK-715
产品别名：TAK-715

生物活性：

Description

TAK-715 is a p38 MAPK inhibitor for p38α with IC50 of 7.1 nM, 28-fold more selective for p38α over p38β, no inhibition to p38γ/δ, JNK1, ERK1, IKKβ, MEKK1 or TAK1. IC50 value: 7.1 nM [1] Target: p38α MAPK in vitro: TAK 715 inhibits LPS-stimulated release of TNF-alpha from THP-1 with IC50 of 48 nM [1]. TAK 715 (10 μM) inhibits Wnt-3a-induced hDvl2 phosphorylation and the hDvl2 shift in U2OS-EFC cells [2]. The amide NH of TAK 715 is hydrogen bonded to the main-chain carbonyl of Met109 of p38 alpha. TAK 715 binds relatively high in the ATP pocket, occupying the hydrophobic back pocket, the adenine region and the front pocket of p38 as well as extending to most of the length of the Gly-rich loop [3]. in vivo: TAK 715 (10 mg/kg, po) inhibits LPS-induced TNF-alpha production in mice with 87.6% inhibition. TAK 715 has a modest mouse bioavailability of 18.4% and a slightly improved rat bioavailability of 21.1%. TAK 715 has a modest mouse bioavailability of 18.4% and a slightly improved rat bioavailability of 21.1%. TAK 715 results in Cmax of 0.19 μg/mL and AUC(0-24 hours) of 1.16 μg·h/mL in rats. TAK 715 (30 mg/kg, po) significantly reduces the secondary paw volume with 25 % inhibition in a rat adjuvant-induced arthritis (AA) model [1].

Solvent&Solubility

In Vitro:

DMSO : ≥ 100 mg/mL (**250.31 mM**)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" 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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (6.26 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (6.26 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

2.请依序添加每种溶剂： 10% DMSO →90% corn oil

Solubility: ≥ 2.5 mg/mL (6.26 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (6.26 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的

	实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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/?. Chem Biol, 2011, 18(4), 485-494.