产品名称：8-[4-(1-氨基环丁基)苯基]-9-苯基-1,2,4-三唑并[3,4-f][1,6]萘啶-3(2H)-酮二盐酸盐

产品别名：MK-2206 2HCl；MK-2206 dihydrochloride

生物活性：				
Description	MK-2206 dihydrochloride (MK-2206 (2HCl)) is an orally active allosteric AKT inhibitor with IC50s of 5 nM, 12 nM, and 65 nM for AKT1, AKT2, and AKT3, respectively[1].			
IC_{50} & Target	Akt1	Akt2	Akt3	Autophagy
	5 nM (IC_{50})	12 nM (IC_{50})	65 nM (IC_{50})	
In Vitro	MK-2206 dihydrochloride (MK-2206 (2HCl)) (0-10 μM; 72 and 96 hours) inhibits the nasopharyngeal carcinoma (NPC) cell lines CNE-1, CNE-2, HONE-1, and SUNE-1 proliferation in dose- and time-dependent manner[1]. MK-2206 dihydrochloride (0-10 μM; 24 and 48 hours) results in a dose-dependent increase in the percentage of cells in G0/G1 phase and a concomitant reduction of cell numbers in S phase in CNE-2 and HONE-1 cells[1]. MK-2206 dihydrochloride (0-10 μM; 24 hours) attenuates phosphorylation levels of PRAS40 and S6 in a dose-dependent manner. MK-2206 does not effect phosphorylation of GSKα/β and AKT[1]. MK-2206 dihydrochloride (0-10 μM; 24 hours) increases the appearance of LC3-II in CNE-2 cells dose-dependently. Microtubule-associated protein 1 LC3 is an essential autophagy protein[1].			
	Cell Proliferation Assay[1]			
	Cell Line:	The NPC cell lines CNE-1, CNE-2, HONE-1, and SUNE-1		
	Concentration:	0.08, 0.16, 0.31, 0.63, 1.25, 2.5, 5, 10 μM		
	Incubation Time:	72 and 96 hours		
	Result:	At 72 and 96 hours, the IC_{50} values in CNE-1, CNE-2, and HONE-1 cell lines were 3-5 μM, and in SUNE-1, they were less than 1 μM.		
	Cell Cycle Analysis[1]			
	Cell Line:	CNE-2 and HONE-1 cells		
	Concentration:	0.625, 1.25, 2.5, 5, 10 μM		
	Incubation Time:	24 or 48 hours		
	Result:	Induced cell cycle arrest at G1 in a dose-dependent manner.		
	Western Blot Analysis[1]			
	Cell Line:	SUNE-1 and CNE-2 cells		
	Concentration:	0.625, 1.25, 2.5, 5, 10 μM		
	Incubation Time:	24 hours		
	Result:	Inhibited phosphorylation of AKT downstream targets.		
	Cell Autophagy Assay[1]			
	Cell Line:	CNE-2 cells		
	Concentration:	0.625, 1.25, 2.5, 5, 10 μM		
	Incubation Time:	24 hours		
	Result:	Induced autophagy.		
In Vivo	Both MK-2206 dihydrochloride (MK-2206 (2HCl)) doses (oral gavage; 480 mg/kg once a week and 240 mg/kg three times a week; for 2 weeks) can inhibit the growth of human CNE-2 xenografts in nude mice. In the two MK-2206 dihydrochloride groups, the tumor weights are much lighter than the control group.			

	Temporal body weight reduction is observed after receiving the MK-2206 dihydrochloride treatment[1]. No other obvious toxicity is observed in mice[1]. MK-2206 dihydrochloride (orally; 120 mg/kg; alternate days; for 3 weeks) significantly inhibits tumor growth[2].

Animal Model:	Four- to 6-week-old male BALB/c nude mice with CNE-2 xenografts[1]
Dosage:	240 mg/kg and 480 mg/kg
Administration:	Oral gavage; 240 mg/kg for three times a week; 480 mg/kg for once a week; for 2 weeks
Result:	Both doses inhibited the growth of human CNE-2 xenografts in nude mice.

Solvent&Solubility

In Vitro:

DMSO : 20 mg/mL (41.63 mM; Need ultrasonic)

H_2O : 3.81 mg/mL (7.93 mM; Need ultrasonic and warming)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0816 mL	10.4082 mL	20.8164 mL
	5 mM	0.4163 mL	2.0816 mL	4.1633 mL
	10 mM	0.2082 mL	1.0408 mL	2.0816 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 mg/mL (4.16 mM); Clear solution

此方案可获得 ≥ 2 mg/mL (4.16 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 20.0 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% (20% SBE-β-CD in saline)

Solubility: ≥ 2 mg/mL (4.16 mM); Clear solution

此方案可获得 ≥ 2 mg/mL (4.16 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 20.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。

References

[1]. Zhao YY, et al. Effects of an oral allosteric AKT inhibitor (MK-2206) on human nasopharyngeal cancer in vitro and in vivo. Drug Des Devel Ther. 2014 Oct 10;8:1827-37.

[2]. Agarwal E, et al. Akt inhibitor MK-2206 promotes anti-tumor activity and cell death by modulation of AIF and Ezrin in colorectal cancer. BMC Cancer. 2014 Mar 1;14:145.