产品名称：INCB 024360
产品别名：Epacadostat

生物活性：

Description	Epacadostat (INCB 024360) is a potent and selective **indoleamine 2,3-dioxigenase 1 (IDO1)** inhibitor with an **IC_{50}** of 71.8 nM.
IC_{50} & Target	IDO1
	71.8 nM (IC_{50})
In Vitro	In cellular assays, Epacadostat (INCB 024360) selectively inhibits human IDO1 with IC50 values of approximately 10 nM, demonstrating little activity against other related enzymes such as IDO2 or tryptophan 2,3-dioxygenase (TDO). Epacadostat (INCB 024360) also exhibits significant activity toward mouse IDO1, with an IC50 value of 52.4 nM±15.7 nM, in a similar assay using mouse IDO1-transfected HEK293/MSR cells[1].
In Vivo	Female Balb/c mice bearing CT26 tumors are treated orally twice daily for 12 d with Epacadostat at 100 mg/kg. Epacadostat (INCB 024360) suppresses kynurenine equivalently in plasma, tumors, and lymph nodes. In naïve C57BL/6 mice, 50 mg/kg Epacadostat (INCB 024360) decreases plasma kynurenine levels within 1 hour and those levels stay at least 50% suppressed through the 8-hour time course[2].

Solvent&Solubility

In Vitro:

DMSO : 100 mg/mL (**228.19 mM;** Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2819 mL	11.4095 mL	22.8191 mL
	5 mM	0.4564 mL	2.2819 mL	4.5638 mL
	10 mM	0.2282 mL	1.1410 mL	2.2819 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 (5.70 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.70 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% (20% SBE-β-CD in saline)

Solubility: ≥ 2.5 mg/mL (5.70 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.70 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 900 μL 20% 的 SBE-β-CD 生理

	盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (5.70 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.70 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]. Liu X, et al. Selective inhibition of IDO1 effectively regulates mediators of antitumor immunity. Blood. 2010 Apr 29;115(17):3520-30. [2]. Koblish HK, et al. Hydroxyamidine inhibitors of indoleamine-2,3-dioxygenase potently suppress systemic tryptophan catabolism and the growth of IDO-expressing tumors. Mol Cancer Ther. 2010 Feb;9(2):489-98. [3]. Fu R, et al. LW106, a novel indoleamine 2,3-dioxygenase 1 inhibitor, suppresses tumour progression by limiting stroma-immune crosstalk and cancer stem cell enrichment in tumour micro-environment. Br J Pharmacol. 2018 Jul;175(14):3034-3049.

实验参考：

Cell Assay	To determine Epacadostat activity against IDO in recombinant cells, HEK293/MSR cells are transiently transfected with full-length human or mouse IDO1, or mouse IDO2 cDNA, with Transit-293 transfection reagent or Lipofectamine 2000 reagents. Epacadostat (INCB 024360) at different concentrations is added to the recovered transfected cells seeded at 2×10^4 cells per well in a 96-well plate (200 μL/well). The cells are incubated for 2 days, and kyn in the supernatants is measured as described in the HeLa cell assay. The tryptophan 2,3-dioxygenase (TDO) assay is performed similarly with HEK293/MSR cells transfected with a human TDO expression vector[1].
Animal Administration	Mice[2] The female C57BL/6 mice are dosed orally with 50 mg/kg Epacadostat. C57BL/6 wild-type or Ido1$^{-/-}$deficient mice are administered a single oral dose of Epacadostat (INCB 024360), at which point food is removed from the cages until after the 8-h time point. At various time points after dosing, mice are euthanized and blood is collected by cardiac puncture. Plasma is analyzed for the presence of Epacadostat (INCB 024360), tryptophan, and kynurenine according to the methods below.
References	[1]. Liu X, et al. Selective inhibition of IDO1 effectively regulates mediators of antitumor immunity. Blood. 2010 Apr 29;115(17):3520-30. [2]. Koblish HK, et al. Hydroxyamidine inhibitors of indoleamine-2,3-dioxygenase potently suppress systemic tryptophan catabolism and the growth of IDO-expressing tumors. Mol Cancer Ther. 2010 Feb;9(2):489-98. [3]. Fu R, et al. LW106, a novel indoleamine 2,3-dioxygenase 1 inhibitor, suppresses tumour progression by limiting stroma-immune crosstalk and cancer stem cell enrichment in tumour micro-environment. Br J Pharmacol. 2018 Jul;175(14):3034-3049.