产品名称：**PF-5274857**
产品别名：**PF-5274857**

生物活性：

Description

PF-5274857 is a potent and selective Smoothened (Smo) antagonist, inhibits Hedgehog (Hh) signaling with IC50 and Ki of 5.8 nM and 4.6 nM, respectively, and can penetrate the blood–brain barrier. IC50 value: 5.8 nM Target: Smoothened in vitro: PF-5274857 completely inhibits Shh-induced Hh pathway activity with IC50 of 2.7 nM measured by the transcriptional activity of Smo downstream gene Gli1 in MEF cells. The μ-opioid receptor is weakly inhibited by PF-5274857 with a dissociation constant of 36 μM subsequently determined in a functional assay [1]. in vivo: PF-5274857 shows significant dose-dependent tumor growth inhibition (TGI) and induces tumor regression at high doses(>10 mg/kg)., PF-5274857 downregulates Gli1, Gli2, Ptch1, and Ptch2 gene expression levels to various degrees with maximal effects being achieved between 6 and 12 hours post-dose (Gli1 is the most sensitive gene), whereas PF-5274857 has little effect on Smo levels. In skin tissue, downregulation of Gli1 and Gli2 is also observed with a similar time course by PF-5274857. The model-derived drug concentration for half maximal inhibition of the tumor Gli1 mRNA production rate (IC50) by PF-5274857 is determined to be 8.9 nM in the Ptch+/?p53+/? medulloblastoma allograft mice, which mathematically corresponds to tumor regression of 119% TGI after 6 days of plasma exposure at this concentration. In the Ptch+/?p53?/? medulloblastoma allograft mice, the IC50 value is estimated to be 3.5 nM, consistent with the Ptch+/?p53+/? results. PF-5274857 is also able to cross the blood–brain barrier in rats within 4 hours post-dose [1].

Solvent&Solubility

In Vitro:

DMSO : 125 mg/mL (**286.07 mM;** Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2885 mL	11.4427 mL	22.8854 mL
5 mM	0.4577 mL	2.2885 mL	4.5771 mL
10 mM	0.2289 mL	1.1443 mL	2.2885 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: ≥ 2.08 mg/mL (4.76 mM); Clear solution

此方案可获得 ≥ 2.08 mg/mL (4.76 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 20.8 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: ≥ 2.08 mg/mL (4.76 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (4.76 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 20.8 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: ≥ 2.08 mg/mL (4.76 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (4.76 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 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Rohner A, et al. Effective targeting of Hedgehog signaling in a medulloblastoma model with PF-5274857, a potent and selective Smoothened antagonist that penetrates the blood-brain barrier. Mol Cancer Ther. 2012, 11(1), 57-65.