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产品名称：JNJ-42041935
产品别名：JNJ-42041935

生物活性：

Description	JNJ-42041935 is a potent, competitive and selective inhibitor of prolyl hydroxylase PHD; inhibits PHD1, PHD2, and PHD3 with pK_i values of 7.91±0.04, 7.29 ±0.05, and 7.65±0.09, respectively.
IC_{50} & Target	pKi: 7.91±0.04 (PHD1), 7.29 ±0.05 (PHD2), 7.65±0.09(PHD3)[1]
In Vitro	JNJ-42041935 is the most potent inhibitor of $PHD2_{181–417}$ with a pIC_{50} value of 7.0±0.03. JNJ-42041935 also inhibits full-length PHD1, PHD2, and PHD3 enzymes (pKi values 7.91±0.04, 7.29 ±0.05, and 7.65±0.09, respectively) [1].
In Vivo	JNJ-42041935 is used to compare the effect of selective inhibition of PHD to intermittent, high doses (50 μg/kg i.p.) of an exogenous erythropoietin receptor agonist in an inflammation induced anemia model in rats. JNJ-42041935 (100 μmol/kg, once a day for 14 days) is effective in reversing inflammation induced anemia, whereas erythropoietin has no effect. Administration of JNJ-42041935 (100 μmol/kg p.o.) for 5 consecutive days resulted in a 2-fold increase in reticulocytes, an increase in hemoglobin by 2.3 g/dl, and an increase in the hematocrit of 9%. Two hours after oral administration of 300 μmol/kg JNJ-42041935, the bioluminescence over the peritoneal area is increased by 2.2 ± 0.3-fold relative to luciferase-treated vehicle controls in the mouse [1].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 36 mg/mL (103.85 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.8848 mL	14.4238 mL	28.8475 mL
5 mM	0.5770 mL	2.8848 mL	5.7695 mL
10 mM	0.2885 mL	1.4424 mL	2.8848 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 (7.21 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (7.21 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 (7.21 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (7.21 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 (7.21 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (7.21 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]. Barrett TD, et al. Pharmacological characterization of 1-(5-chloro-6-(trifluoromethoxy)-1H-benzoimidazol-2-yl)-1H-pyrazole-4-carboxylic acid (JNJ-42041935), a potent and selective hypoxia-inducible factor prolyl hydroxylase inhibitor. Mol Pharmacol. 2011

实验参考：

Animal Administration	Mice: JNJ-42041935 is administered at doses of 30, 100, and 300 μmol/kg to Balb/C mice . Plasma is collected 6 h after the dose. Plasma erythropoietin concentration is measured. The hematological effects of JNJ-42041935 are assessed by administering the 100 μmol/kg dose on 5 consecutive days and collecting blood anticoagulated with EDTA on day 8 (3 days after the last dose)[1].
Kinase Assay	The potency of JNJ-42041935 for inhibition of the structurally related enzyme FIH is assessed by methods similar to those described for PHD2. In brief, activity of FIH is determined using purified glutathione transferase-tagged full-length FIH amino acids 1 to 350 and a synthetic HIF-1α peptide corresponding to residues Asp788 to Leu822. Compounds are preincubated with 17.1 nM FIH for 30 min, followed by a 10-min incubation with 1 μM [2-^{14}C]2-oxoglutarate, in the presence of 10 μM $FeNH_4SO_4$ in reaction buffer. The selectivity of JNJ-42041935 for inhibition of a range of other targets available for testing in commercial assays is also assessed at concentrations of 1 and 10 μM[1].
References	[1]. Barrett TD, et al. Pharmacological characterization of 1-(5-chloro-6-(trifluoromethoxy)-1H-benzoimidazol-2-yl)-1H-pyrazole-4-carboxylic acid (JNJ-42041935), a potent and selective hypoxia-inducible factor prolyl hydroxylase inhibitor. Mol Pharmacol. 2011