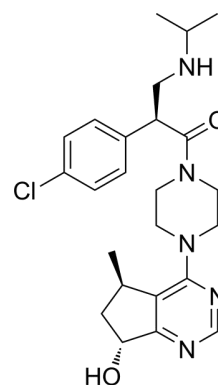


Ipatasertib(pan-Akt 抑制剂)

货号: RPM0019

◆ 产品信息

中文名称/Chinese Name:	Ipatasertib(pan-Akt 抑制剂)
别称/Synonyms:	GDC-0068, RG7440, 帕他色替
CAS 号/CAS NO.:	1001264-89-6
化学式/Formula:	C ₂₄ H ₃₂ ClN ₅ O ₂
分子量/M.Wt:	458
外观/Appearance:	固体
保存条件/Storage:	Powder: -20°C, 3 年 Insolvent: -80°C, 1 年



◆ 溶解信息

溶解度/Solubility:	DMSO: 85 mg/mL (185.6 mM). Ethanol: 85 mg/mL (185.6 mM) H2O: < 1 mg/mL (<1mg/ml 是指产品微溶或不溶)
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溶液配制参考/Preparing Stock Solutions:

	1 mg	5 mg	10 mg
1 mM	2.1834 mL	10.917 mL	21.8341 mL
5 mM	0.4367 mL	2.1834 mL	4.3668 mL
10 mM	0.2183 mL	1.0917 mL	2.1834 mL
50 mM	0.0437 mL	0.2183 mL	0.4367 mL

◆ 生物活性

产品描述/Description	Ipatasertib(pan-Akt 抑制剂) 是选择性的, ATP 竞争性的 pan-Akt 抑制剂, 能够抑制 Akt1 (IC ₅₀ :5 nM), Akt2 (IC ₅₀ :18 nM), Akt3 (IC ₅₀ :8 nM)。Ipatasertib(pan-Akt 抑制剂)可以通过抑制 Akt 导致 p53 非依赖性 PUMA 激活, 从而同步激活 FoxO3a 和 NF-κB, 直接与 PUMA 启动子结合, 上调 PUMA 转录和 Bax 介导的线粒体凋亡。
靶点活性/Targets (IC ₅₀)	Akt1:5 nM (IC ₅₀);Akt3:8 nM (IC ₅₀);Akt2:18 nM (IC ₅₀); PKA: 3100 nM (IC ₅₀)
体外活性/In vitro	1. Ipatasertib (10 μM; 12, 24 h) 在细胞实验中, 通过非 p53 依赖性的 PUMA 激活抑制结肠癌细胞增殖 ^[1] 。 2. Ipatasertib (1, 5, 10, 20 μM; 24 h/10 μM; 3, 6, 12, 24 h) 在

	HCT116 细胞中，以时间和浓度依赖的方式上调 PUMA 的表达^[1]。 3. Ipatasertib 在野生型、p53-/- 型，以及 DLD1 (p53 突变) 型 HCT116 细胞中增加 PUMA 的 mRNA 水平^[1]。 4. Ipatasertib (10 μM; 24 h) 通过 PUMA/Bax 途径诱导 HCT116 细胞凋亡^[1]。
体内活性/In vivo	1. Ipatasertib (30 mg/kg; p.o.; single daily for 15 consecutive days) 在野生型和 PUMA-/- 型 HCT116 异种移植小鼠模型中显示出 PUMA 依赖性抗肿瘤活性^[1]。
激酶实验/Kinase Assay	1. The fluorescence polarization assay for ATP competitive inhibition is done as follows: mPI3Kα dilution solution (90 nM) is prepared in fresh assay buffer (50 mM Hepes pH 7.4, 150 mM NaCl, 5 mM DTT, 0.05% CHAPS) and kept on ice. The enzyme reaction contains 0.5 nM mouse PI3Kα (p110α/p85α complex purified from insect cells), 30 μM PIP2, PF-04691502 (0, 1, 4, and 8 nM), 5 mM MgCl₂, and 2-fold serial dilutions of ATP (0–800 μM). Final dimethyl sulfoxide is 2.5%. The reaction is initiated by the addition of ATP and terminated after 30 minutes with 10 mM EDTA. In a detection plate, 15 μL of detector/probe mixture containing 480 nM GST-Grp1PH domain and 12 nM TAMRA tagged fluorescent PIP3 in assay buffer is mixed with 15 μL of kinase reaction mixture. The plate is shaken for 3 minutes, and incubated for 35 to 40 minutes before reading on an LJL Analyst HT.
细胞实验/Cell Research	1. GDC-0068 is prepared in DMSO and stored, and then diluted with appropriate medium before use^[2]. The 384-well plates are seeded with 2,000 cells per well in a volume of 54 μL per well followed by incubation at 37°C under 5% CO₂ overnight (~16 hours). Compounds (e.g., GDC-0068) are diluted in DMSO to generate the desired stock concentrations then added in a volume of 6 μL per well. All treatments are tested in quadruplicates. After 4 days incubation, relative numbers of viable cells are estimated using CellTiter-Glo and total luminescence is measured on a Wallac Multilabel Reader. The concentration of drug resulting in IC₅₀ is calculated from a 4-parameter curve analysis (XLfit) and is determined from a minimum of 3 experiments. For cell lines that failed to achieve an IC₅₀, the highest concentration tested (10 μM) is listed^[2].

◆ 参考文献

[1] Sun L, et al. Ipatasertib, a novel Akt inhibitor, induces transcription factor FoxO3a and NF- κ B directly regulates PUMA-dependent apoptosis. Cell Death Dis. 2018 Sep 5;9(9):911.

[2] Blake JF, et al. Discovery and preclinical pharmacology of a selective ATP-competitive Akt inhibitor (GDC-0068) for the treatment of human tumors. J Med Chem. 2012 Sep 27;55(18):8110–27.

◆ 注意事项

1. 请在收到本产品后立即按照说明书中推荐的条件保存，使用前进行离心，使粉末充分沉降于管底。
2. 请根据实验目的及本产品的溶解性，选择相应的溶剂配制高浓度母液后使用，最佳工作浓度请参考相关文献通过实验摸索优化，本说明书中的数据来源于公开文献，仅供参考。
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4. 为了您的安全和健康，请穿实验服并戴一次性手套操作。