产品名称：2-氨基-N-[2,3-二氢-7-甲氧基-8-[3-(4-吗啉基)丙氧基]咪唑并[1,2-C]喹唑啉-5-基]-5-嘧啶甲酰胺

产品别名：Copanlisib BAY 80-6946；库潘尼西

生物活性：

Description	Copanlisib (BAY 80-6946) is a potent, selective and ATP-competitive pan-class I PI3K inhibitor, with IC50s of 0.5 nM, 0.7 nM, 3.7 nM and 6.4 nM for PI3Kα, PI3Kδ, PI3Kβ and PI3Kγ, respectively. Copanlisib has more than 2,000-fold selectivity against other lipid and protein kinases, except for mTOR. Copanlisib has superior antitumor activity[1].				
IC_{50} & Target	PI3Kα	PI3Kδ	PI3Kβ	PI3Kγ	mTOR
	0.5 nM (IC_{50})	0.7 nM (IC_{50})	3.7 nM (IC_{50})	6.4 nM (IC_{50})	45 nM (IC_{50})

In Vitro	Copanlisib (BAY 80-6946; 20-200 nM; 24 hours; BT20 breast cancer cells) treatmemnt induces apoptosis in a subset of tumor cell lines that are resistant to Lapatinib and Trastuzumab[1]. Copanlisib (BAY 80-6946; 0.5-500 nM; 2 hours; ELT3 cells) treatmemnt shows complete inhibition of PI3K-mediated AKT phosphorylation in ELT3 cells[1]. Copanlisib potently inhibits cell proliferation in a panel of human tumor cell lines. Copanlisib has mean IC50 values of 19 nM against cell lines with PIK3CA-activating mutations and 17 nM against HER2-positive cell lines, whereas the activity in PIK3CA wild-type and HER2-negative cells is about 40-fold less potent[1].	
	Apoptosis Analysis[1]	
	Cell Line:	BT20 breast cancer cells
	Concentration:	20 nM and 62 nM, 200 nM
	Incubation Time:	24 hours
	Result:	Significantly increased caspase9 activities. Also increased levels of phosphorylated p53 at Ser15and cleaved PARP. Induced caspase-9 activation with an **EC_{50}** of 340 nM.
	Western Blot Analysis[1]	
	Cell Line:	ELT3 cells
	Concentration:	0.5 nM, 5 nM, 50 nM, 500 nM
	Incubation Time:	2 hours
	Result:	Complete inhibition of PI3K-mediated AKT phosphorylation was clearly shown at a concentration of 5 nM.

In Vivo	Copanlisib (BAY 80-6946; 0.5-6 mg/kg; intravenous injection; every second day, every third day; for 60 days; athymic nude rats) treatment displays robust antitumor activity in the rat KPL4 tumor xenograft model[1].	
	Animal Model:	Athymic nude rats injected with KPL4 tumor cells[1]
	Dosage:	0.5 mg/kg, 1 mg/kg, 3 mg/kg or 6 mg/kg
	Administration:	Intravenous injection; every second day, every third day; for 60 days
	Result:	On day 25, tumor growth inhibition (TGI) rates of 77%, 84%, 99%, and 100% were observed at doses of 0.5, 1, 3, and 6 mg/kg, respectively. All rats remained tumor free at the termination of the study on day 73.
	In Vitro:	

<table>
<tr><td>Solvent&Solubility</td><td colspan="5">1M HCl : 100 mg/mL (208.11 mM; Need ultrasonic)
DMSO : < 1 mg/mL (insoluble or slightly soluble)
H_2O : < 0.1 mg/mL (insoluble)</td></tr>
<tr><td rowspan="4"></td><td rowspan="4">Preparing Stock Solutions</td><td>Solvent / Mass / Concentration</td><td>1 mg</td><td>5 mg</td><td>10 mg</td></tr>
<tr><td>1 mM</td><td>2.0811 mL</td><td>10.4054 mL</td><td>20.8108 mL</td></tr>
<tr><td>5 mM</td><td>0.4162 mL</td><td>2.0811 mL</td><td>4.1622 mL</td></tr>
<tr><td>10 mM</td><td>0.2081 mL</td><td>1.0405 mL</td><td>2.0811 mL</td></tr>
<tr><td colspan="5">*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。</td></tr>
<tr><td>References</td><td colspan="5">[1]. Liu N, et al. BAY 80-6946 is a highly selective intravenous PI3K inhibitor with potent p110α and p110δ activities in tumor cell lines and xenograft models. Mol Cancer Ther. 2013 Nov;12(11):2319-30.</td></tr>
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