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产品名称：Vericiguat
产品别名： BAY1021189

生物活性：

Description	Vericiguat (BAY1021189) is a potent, orally available and soluble guanylate cyclase stimulator.
In Vitro	Vericiguat (0.01 μM to 100 μM) stimulates recombinant sGC concentration dependently, by 1.7-fold to 57.6-fold. When combined with the NO donor diethylamine/nitric oxide complex (DEA/NO), vericiguat and DEA/NO have a synergistic effect on the enzyme activity over a wide range of concentrations. At highest concentrations of vericiguat (100 μM) and DEA/NO (100 nM), the specific activity of sGC is 341.6-fold above baseline. Vericiguat stimulates the sGC reporter cell line concentration dependently, with an EC_{50} of 1005±145 nM. Vericiguat inhibits phenylephrine-induced contractions of rabbit saphenous artery rings, rabbit aortic rings, and canine femoral vein rings concentration dependently, with IC_{50} values of 798, 692, and 3072 nM, respectively. Vericiguat inhibits the U46619-induced contractions of porcine coronary artery rings concentration dependently, with an IC_{50} of 956 nM[1].
In Vivo	Chronic oral treatment with 3 or 10 mg/kg vericiguat qd results in a significant attenuation of blood pressure increase during the course of the study. However, the overall rise of blood pressure increase is not halted in the 3 and 10 mg/kg treatment groups. Vericiguat treatment at 3 or 10 mg/kg leads to a significant reduction in kidney injury molecule Kim-1 and osteopontin expression which are used as biomarkers for renal injury and dysfunction. Vericiguat results in a significant and dose-dependent increase in survival rates. In the 3 and 10 mg/kg qd treatment groups, the rat survival rate is 70% and 90%, respectively, at the study end[1].
Solvent&Solubility	***In Vitro:*** **DMSO : 60 mg/mL** (**140.72 mM;** Need ultrasonic) **H_2O : < 0.1 mg/mL** (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3453 mL	11.7266 mL	23.4533 mL
5 mM	0.4691 mL	2.3453 mL	4.6907 mL
10 mM	0.2345 mL	1.1727 mL	2.3453 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 (5.86 mM); Clear solution

	此方案可获得 ≥ 2.5 mg/mL (5.86 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。
References	[1]. Follmann M, et al. Discovery of the Soluble Guanylate Cyclase Stimulator Vericiguat (BAY 1021189) for the Treatment of Chronic Heart Failure. J Med Chem. 2017 Jun 22;60(12):5146-5161.

实验参考：

Animal Administration	Rats: Rat are randomly allocated to three study groups: placebo (control), 24 low dose, and 24 high dose (3 and 10 mg/kg per day, respectively, administered po by gavage qd). Blood pressure is measured via the tail-cuff method once before the start of the study (day 0) to exclude preexisting differences between the groups and on day 7, 14, and 21. Body weight and survival are assessed on day 1, 8, and 15 and at the study end. At the end of the study (day 22), all animals are anesthetized, blood is collected, and animals are sacrificed; blood is taken in order to assess plasma parameters, and the heart is dissected into the left and right ventricles and is weighed to assess potential heart hypertrophy. Creatinine, urea, and renin activity in plasma are determined after extraction[1].
References	[1]. Follmann M, et al. Discovery of the Soluble Guanylate Cyclase Stimulator Vericiguat (BAY 1021189) for the Treatment of Chronic Heart Failure. J Med Chem. 2017 Jun 22;60(12):5146-5161.