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产品名称：N-[4-[[6-[4-(三氟甲基)苯基]-4-嘧啶基]氧基]-2-苯并噻唑基]乙酰胺
产品别名：AMG 517

生物活性：

Description	AMG 517 is a potent and selective vanilloid receptor-1 (TRPV1) antagonist with an IC50 of 0.5 nM.
IC_{50} & Target	IC50: 0.5 nM (TRPV1)[1]
In Vitro	AMG 517 retains potency in the capsaicin- and acid-mediated assays with IC_{50} values of 0.9 and 0.5 nM[1]. AMG 517 inhibits capsaicin, pH 5, and heat-induced $^{45}Ca^{2+}$ uptake into cells expressing TRPV1 with IC_{50} values of 1 to 2 nM. AMG 517 blocks capsaicin-, proton-, and heat-induced inward currents in TRPV1-expressing cells similarly. AMG 517 inhibits native TRPV1 activation by capsaicin in rat dorsal root ganglion neurons with an IC50 value of 0.68 ± 0.2 nM. AMG 517 is a competitive antagonist of both rat and human TRPV1 with dissociation constant (Kb) values of 4.2 and 6.2 nM, respectively[2].
In Vivo	AMG 517 is shown to be effective in a rodent “on-target” biochemical challenge model (capsaicin-induced flinch, ED50=0.33 mg/kg p.o.) and is antihyperalgesic in a model of inflammatory pain (CFA-induced thermal hyperalgesia, MED=0.83 mg/kg, p.o.)[1].The minimally effective dose is 0.3 mg/kg for AMG 517 and the corresponding plasma concentration is 90 ng/mL. Oral administration of AMG 517 reverses established thermal hyperalgesia in a dose-dependent manner at 21 h after CFA injection. AMG 517 causes transient hyperthermia in rodents, dogs, and monkeys. AMG 517 induces hyperthermia in a steep dose-dependent manner, with 0.3, 1, and 3 mg/kg associated with 0.5, 0.6, and 1.6°C increases in body temperature, respectively. Body temperatures of rats treated with all doses of AMG 517 return to baseline within 10 to 20 h[2].
Solvent&Solubility	***In Vitro:*** **DMSO : 12.91 mg/mL (30.00 mM;** Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3234 mL	11.6171 mL	23.2342 mL
5 mM	0.4647 mL	2.3234 mL	4.6468 mL
10 mM	0.2323 mL	1.1617 mL	2.3234 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 (5.81 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.81 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% corn oil Solubility: ≥ 2.5 mg/mL (5.81 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.81 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]. Doherty EM, et al. Novel vanilloid receptor-1 antagonists: 2. Structure-activity relationships of 4-oxopyrimidines leading to the selection of a clinical candidate. J Med Chem. 2007 Jul 26;50(15):3515-27. [2]. Gavva NR, et al. Repeated administration of vanilloid receptor TRPV1 antagonists attenuates hyperthermia elicited by TRPV1 blockade. J Pharmacol Exp Ther. 2007 Oct;323(1):128-37.

实验参考：

Animal Administration	Rats: After multiple days of full habituation to the testing equipment and paradigm, CFA-induced thermal hyperalgesia is evaluated by measuring paw withdrawal latencies in male Sprague-Dawley rats. Twenty-one hours after CFA injection (50 μL of 0.1%), animals are dosed (p.o.) with AMG 517 or AMG8163 at a dose range of 0.001 to 30 mg/kg in a volume of 5 mL/kg. Two hours after drug dosing (23 h after CFA injection), paw withdrawal latencies are measured using modified Hargreaves hot boxes by investigators fully blinded to treatment conditions[2].
References	[1]. Doherty EM, et al. Novel vanilloid receptor-1 antagonists: 2. Structure-activity relationships of 4-oxopyrimidines leading to the selection of a clinical candidate. J Med Chem. 2007 Jul 26;50(15):3515-27. [2]. Gavva NR, et al. Repeated administration of vanilloid receptor TRPV1 antagonists attenuates hyperthermia elicited by TRPV1 blockade. J Pharmacol Exp Ther. 2007 Oct;323(1):128-37.