产品名称：MK-3207 (Hydrochloride)
产品别名：MK-3207 Hydrochloride

生物活性：

Description	MK-3207 (Hydrochloride) is a potent and orally bioavailable CGRP receptor antagonist with IC_{50} of 0.12 nM and K_i of 0.024 nM, and is highly selective versus human AM1, AM2, CTR, and AMY3.
IC_{50} & Target	IC50: 0.12 nM (CGRP receptor)
In Vitro	MK-3207 displays a similar affinity (K_i) for the rhesus monkey receptor (0.024±0.001 nM; n=14) as for human, but it displays >400-fold lower affinity for the canine and rat receptors, with values of 10 nM and 10±1.2 nM, respectively. MK-3207 is highly selective versus the human AM1 (CLR/RAMP2) and AM2 (CLR/RAMP3) receptors, with K_i values of 16,500 nM and 156±17 nM, respectively. MK-3207 maintains a high degree of selectivity versus human CTR, with a K_i value of 1.9±0.58 μM. MK-3207 also displays good selectivity versus the AMY3 (CTR/RAMP3) receptor, with a $K_i$value of 128±25 nM, but it is less selective versus the AMY1 (CTR/RAMP1) receptor, with a K_i value of 0.75±0.13 nM. MK-3207 potently blocks human α-CGRP-stimulated cAMP responses in human CGRP receptor-expressing HEK293 cells, with an IC_{50} value of 0.12±0.02 nM. MK-3207 displays significantly lower potency for the rat CGRP receptor, with a pIC_{50}=7.31±0.09 [1]
In Vivo	MK-3207 is CNS-penetrant and therefore significantly engaging central receptors. After an oral dose of 10 mg/kg MK-3207, the CSF/plasma ratio is 2 to 3% [1]
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 100 mg/mL (168.34 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6834 mL	8.4168 mL	16.8336 mL
	5 mM	0.3367 mL	1.6834 mL	3.3667 mL
	10 mM	0.1683 mL	0.8417 mL	1.6834 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 (4.21 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.21 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 (4.21 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.21 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 (4.21 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.21 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]. Salvatore CA, et al. Pharmacological properties of MK-3207, a potent and orally active calcitonin gene-related peptide receptor antagonist. J Pharmacol Exp Ther. 2010 Apr;333(1):152-60.

实验参考：

Animal Administration	A customized flexible silicone catheter is freely suspended in the cisterna magna, anchored firmly on both sides of the atlanto-occipital membrane, and tunneled subcutaneously to the midscapular region where it is fed into a surgically implanted port body. CSF is accessed by aseptically inserting a needle through the skin and membrane covering the port into the reservoir of the port body; blood samples are collected by peripheral venipuncture. After oral administration of MK-3207 at 10 mg/kg (0.5% methylcellulose, with an adjusted pH appr 3) to cisterna magna catheter and port-implanted rhesus monkeys, CSF and plasma samples are collected at 0.5, 1, 2, 4, 8, and 24 h and analyzed for compound levels. [1]
Kinase Assay	Amylin binding assays are conducted by combining MK-3207 and 40 pM ^{125}I-rat amylin, followed by 25 μg of CTR/RAMP1 or 25 μg of CTR/RAMP3 membranes and incubated for 3 h at room temperature in binding buffer (10 mM HEPES, 5 mM $MgCl_2$, and 0.2% bovine serum albumin) in a total volume of 1 mL. Calcitonin binding assays are with 25 μg of CTR membranes and 30 pM ^{125}I-human calcitonin as the radioligand. Incubations are terminated by filtration through GF/B 96-well filter plates that has been blocked with 0.5% polyethylenimine. Data are analyzed using Prism, and the K_i value is determined using the equation $K_i=IC_{50}/1 + ([ligand]/K_D)$. The K_D value for each receptor is determined by saturation binding experiments. [1]
References	[1]. Salvatore CA, et al. Pharmacological properties of MK-3207, a potent and orally active calcitonin gene-related peptide receptor antagonist. J Pharmacol Exp Ther. 2010 Apr;333(1):152-60.