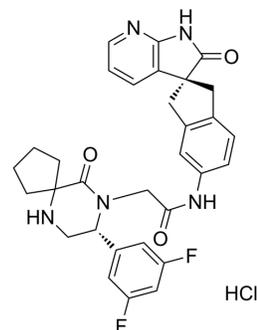


## MK-3207 Hydrochloride

<b>Cat. No.:</b>	HY-10302
<b>CAS No.:</b>	957116-20-0
<b>Molecular Formula:</b>	C <sub>31</sub> H <sub>30</sub> ClF <sub>2</sub> N <sub>5</sub> O <sub>3</sub>
<b>Molecular Weight:</b>	594.05
<b>Target:</b>	CGRP Receptor
<b>Pathway:</b>	GPCR/G Protein; Neuronal Signaling
<b>Storage:</b>	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



### SOLVENT & SOLUBILITY

#### In Vitro

DMSO : ≥ 100 mg/mL (168.34 mM)  
 H<sub>2</sub>O : 50 mg/mL (84.17 mM; Need ultrasonic)  
 \* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		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

Please refer to the solubility information to select the appropriate solvent.

#### In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
Solubility: ≥ 2.5 mg/mL (4.21 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
Solubility: ≥ 2.5 mg/mL (4.21 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil  
Solubility: ≥ 2.5 mg/mL (4.21 mM); Clear solution

### BIOLOGICAL ACTIVITY

#### Description

MK-3207 (Hydrochloride) is a potent and orally bioavailable CGRP receptor antagonist with IC<sub>50</sub> of 0.12 nM and K<sub>i</sub> of 0.024 nM, and is highly selective versus human AM1, AM2, CTR, and AMY3.

#### IC<sub>50</sub> & Target

IC<sub>50</sub>: 0.12 nM (CGRP receptor)

#### In Vitro

MK-3207 displays a similar affinity (K<sub>i</sub>) 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<sup>[1]</sup>.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

#### 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%<sup>[1]</sup>.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## PROTOCOL

#### Kinase Assay <sup>[1]</sup>

Amylin binding assays are conducted by combining MK-3207 and 40 pM <sup>125</sup>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<sub>2</sub>, 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 <sup>125</sup>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.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

#### Animal Administration <sup>[1]</sup>

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.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## CUSTOMER VALIDATION

- Eur J Pharmacol. 2018 Jun 15;829:85-92.
- Vascul Pharmacol. 2017 Mar;90:36-43.
- Pharmacology. 2019;104(5-6):332-341.

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## 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.

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**Caution: Product has not been fully validated for medical applications. For research use only.**

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