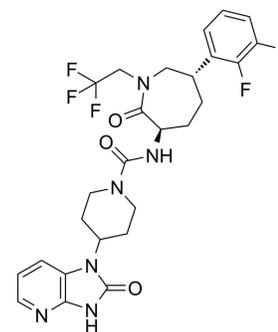


## Telcagepant

<b>Cat. No.:</b>	HY-32709		
<b>CAS No.:</b>	781649-09-0		
<b>Molecular Formula:</b>	C <sub>26</sub> H <sub>27</sub> F <sub>5</sub> N <sub>6</sub> O <sub>3</sub>		
<b>Molecular Weight:</b>	566.52		
<b>Target:</b>	CGRP Receptor		
<b>Pathway:</b>	GPCR/G Protein; Neuronal Signaling		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	2 years
		-20°C	1 year



### SOLVENT & SOLUBILITY

#### In Vitro

DMSO : ≥ 50 mg/mL (88.26 mM)  
 \* "≥" means soluble, but saturation unknown.

	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	1.7652 mL	8.8258 mL	17.6516 mL
	5 mM	0.3530 mL	1.7652 mL	3.5303 mL
	10 mM	0.1765 mL	0.8826 mL	1.7652 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: ≥ 3 mg/mL (5.30 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
Solubility: ≥ 3 mg/mL (5.30 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil  
Solubility: ≥ 3 mg/mL (5.30 mM); Clear solution
- Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline  
Solubility: 2.62 mg/mL (4.62 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)  
Solubility: ≥ 2.62 mg/mL (4.62 mM); Clear solution

### BIOLOGICAL ACTIVITY

#### Description

Telcagepant (MK-0974) is an orally active calcitonin gene-related peptide (CGRP) receptor antagonist with K<sub>i</sub>s of 0.77 nM and 1.2 nM for human and rhesus CGRP receptors, respectively.

<b>IC<sub>50</sub> &amp; Target</b>	Ki: 0.77 nM (human CGRP), 1.2 nM (rhesus CGRP)
<b>In Vitro</b>	Telcagepant (MK-0974) displays affinity (K <sub>i</sub> ) for the canine and rat receptors, with values of 1204 nM and 1192 nM (n=10), respectively. Telcagepant (MK-0974) potently blocks human α-CGRP-stimulated cAMP responses in human CGRP receptor expressing HEK293 cells with an IC <sub>50</sub> of 2.2 nM <sup>[1]</sup> . Telcagepant (MK-0974) displays saturable binding to SK-N-MC membranes with a K <sub>D</sub> of 1.9 nM and B <sub>max</sub> of 479 fmol/mg protein. Telcagepant (MK-0974) also displays saturable binding to rhesus cerebellum homogenate with a K <sub>D</sub> of 1.3 nM and B <sub>max</sub> of 20 fmol/mg <sup>[2]</sup> . MCE has not independently confirmed the accuracy of these methods. They are for reference only.
<b>In Vivo</b>	Telcagepant (MK-0974) (i.v. bolus, 1 mg/kg) demonstrates that the efficacy of this antagonist is time-dependent and correlated with plasma levels <sup>[1]</sup> . The pharmacokinetics of Telcagepant (MK-0974) remains linear across 0.5-10 mg/kg intravenous dose in monkeys, but the oral area under the plasma concentration-time curve (AUC) increase (5-30 mg/kg) is 15-fold over dose-proportional <sup>[3]</sup> . MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## PROTOCOL

<b>Cell Assay</b> <sup>[1]</sup>	HEK293 cells stably transfected with CLR/RAMP1 are plated in complete growth medium at 85,000 cells/well in 96-well poly-D-lysine-coated plates and cultured for 19 h before assay. Cells are washed with PBS and then incubated with inhibitor in the presence or absence of 50% human serum for 30 min at 37°C and 95% humidity in Cellgro Complete Serum-Free/Low-Protein medium with L-glutamine and 1 g/L bovine serum albumin. Isobutylmethylxanthine is added to the cells at a concentration of 300 μM and incubated for 30 min at 37°C. Human α-CGRP is added to the cells at a concentration of 0.3 nM and allowed to incubate at 37°C for 5 min. After α-CGRP stimulation, the cells are washed with PBS and processed for cAMP determination using the two-stage assay procedure according to the manufacturer's recommended protocol. Dose-response curves are plotted, and IC <sub>50</sub> values are determined. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
<b>Animal Administration</b> <sup>[1]</sup>	Monkeys: Rhesus monkeys (male and female) weighing between 4 and 10 kg are used. The right saphenous vein is cannulated for intravenous drug delivery, and blood samples are obtained from the left saphenous artery. Four rubber O-rings (8 mm inner diameter) are placed on the ventral side of the forearm without directly being positioned over a visible vessel. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## CUSTOMER VALIDATION

- Cephalalgia. 2021 Feb 24;333102420983282.
- Vascul Pharmacol. 2017 Mar;90:36-43.

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## REFERENCES

- [1]. Salvatore CA, et al. Pharmacological characterization of MK-0974 [N-[(3R,6S)-6-(2,3-difluorophenyl)-2-oxo-1-(2,2,2-trifluoroethyl)azepan-3-yl]-4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)piperidine-1-carboxamide], a potent and orally active calcitonin receptor-like receptor 1 antagonist. *Journal of Pharmacology and Experimental Therapeutics*. 2011;317(2):405-415.
- [2]. Moore EL, et al. Examining the binding properties of MK-0974: a CGRP receptor antagonist for the acute treatment of migraine. *Eur J Pharmacol*. 2009 Jan 14;602(2-3):250-4.

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[3]. Roller S, et al. Preclinical pharmacokinetics of MK-0974, an orally active calcitonin-gene related peptide (CGRP)-receptor antagonist, mechanism of dose dependency and species differences. *Xenobiotica*. 2009 Jan;39(1):33-45.

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

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