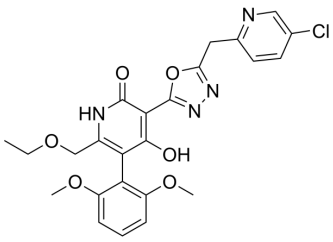
BMS-986224

Cat. No.:	HY-139485
CAS No.:	2055200-88-7
Molecular Formula:	$C_{24}H_{23}ClN_4O_6$
Molecular Weight:	498.92
Target:	Apelin Receptor (APJ)
Pathway:	GPCR/G Protein
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 20.83 mg/mL (41.75 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0043 mL	10.0216 mL	20.0433 mL
	5 mM	0.4009 mL	2.0043 mL	4.0087 mL
	10 mM	0.2004 mL	1.0022 mL	2.0043 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.17 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.17 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BMS-986224 is a potent, selective and orally active APJ receptor agonist (K_d = 0.3 nM). BMS-986224 exhibits similar receptor binding and signaling profile to (Pyr[1]) apelin-13. BMS-986224 has the potential for the research of heart failure[1].

IC_{50} & Target

Kd: 0.3 nM (APJ receptor)[1]

In Vitro

BMS-986224 fully inhibits forskolin-mediated cAMP production, with an EC_{50} for human APJ of 0.02 nM. BMS-986224 (0-100 nM) fully stimulates β-arrestin recruitment, ERK phosphorylation, and APJ internalization in Chinese hamster ovary-K1 or HEK293 ZF cells[1].

BMS-986224 is a potent and selective APJ receptor agonist that exhibits a similar signaling profile to (Pyr1) apelin-13[1].

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

In Vivo

BMS-986224 (0.192 mg/kg or 3 mg/kg; SC infusion; daily;) in the RHR model increased stroke volume and cardiac output to levels seen in healthy animals but without preventing cardiac hypertrophy and fibrosis, effects differentiated from enalapril [1].

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

Animal Model:	Male Sprague-Dawley rats (renal hypertensive rat model)[1]
Dosage:	0.192 mg/kg or 3 mg/kg
Administration:	SC infusion; daily; Initiated 3 days before surgery and continued for 7 days after surgery
Result:	The achieved steady-state plasma concentrations during 10-day infusion were 102 and 2686 nmol/L at low dose and HD, respectively. At the low dose, BMS-986224 increased SV and CO without affecting other measured parameters, including the measured diastolic parameters, cardiac fibrosis, and heart weight in RHR.

REFERENCES

[1]. Gargalovic P, et al. In Vitro and In Vivo Evaluation of a Small-Molecule APJ (Apelin Receptor) Agonist, BMS-986224, as a Potential Treatment for Heart Failure. Circ Heart Fail. 2021;14(3):e007351.

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