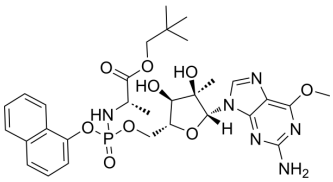
BMS-986094

Cat. No.:	HY-13337
CAS No.:	1234490-83-5
Molecular Formula:	$C_{30}H_{39}N_6O_9P$
Molecular Weight:	658.64
Target:	HCV
Pathway:	Anti-infection
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 : 250 mg/mL (379.57 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.5183 mL	7.5914 mL	15.1828 mL
	5 mM	0.3037 mL	1.5183 mL	3.0366 mL
	10 mM	0.1518 mL	0.7591 mL	1.5183 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.16 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.16 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BMS-986094 (INX-08189) is a potent inhibitor of hepatitis C virus (HCV) replication, with an EC_{50} of 35 nM at 24 h in Huh-7 cells. BMS-986094 is a phosphoramidate proagent of 6-O-methyl-2'-C-methyl guanosine. BMS-986094 can be used for the research of chronic HCV infection[1][2].

IC_{50} & Target

EC50: 35 nM (HCV)[1]

In Vitro

BMS-986094 (INX-08189) is a highly potent inhibitor of HCV replication, with the EC_{50}s of 10 nM against genotype 1b, 12 nM against genotype 1a, and 0.9 nM against genotype 2a after 72 h of exposure. And the concentration resulting in 50% cellular cytotoxicity (CC_{50}) in cultured Huh-7 cells is 7.01 μM[1].

BMS-986094 (5-80 nM; 14 days) decreases luciferase activity in a concentration-dependent manner in genotype 1b replicon

cells[1].
BMS-986094 (20 μM; 3 days) decreases relative mitochondrial copy number of 11% in CEM cells. BMS-986094 (1 μM; 14 days) has no effect on mitochondrial copy number in CEM cells. BMS-986094 does not alter the relative mitochondrial copy number in HepG2 cells[1].
MS-986094 (10 μM; 24 hours) does not increase apparently in the concentration of BMS-986094 or its metabolites in human hepatocytes (HHs) and human cardiomyocytes (HCMs) except that intracellular concentrations of INX-09114 increases and plateaues after a 7-hour incubation in HCM[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

BMS-986094 (3-300 mg/kg; p.o.) converts to 2′-C-Me-GTP after oral administration, and 2'-C-MeG in the plasma is proportional to the production of 2'-C-MeGTP in the liver[1].
BMS-986094 (25 mg/kg; p.o.) is efficiently extracts from the portal circulation by the liver following oral administration in cynomolgus monkeys[1].
BMS-986094 (15 or 30 mg/kg/d; p.o. for 3 weeks) administers cynomolgus monkeys, the nucleoside metabolite M2 was the major plasma analyte, and INX-09114 was the highest drug-related species in the heart and kidney[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male Sprague-Dawley rats[1]
Dosage:	3, 5, 10, 25 mg/kg
Administration:	A single p.o. administration
Result:	At doses of ≥5 mg/kg, the concentrations of 2′-C-MeGTP in the liver exceeded the EC_{90} soon after dosing and remained at or above this level for 72 h.

REFERENCES

[1]. Vernachio JH, et, al. INX-08189, a phosphoramidate prodrug of 6-O-methyl-2'-C-methyl guanosine, is a potent inhibitor of hepatitis C virus replication with excellent pharmacokinetic and pharmacodynamic properties. Antimicrob Agents Chemother. 2011 May; 55(5): 1843-51.

[2]. McGuigan C, et, al. Design, synthesis and evaluation of a novel double pro-drug: INX-08189. A new clinical candidate for hepatitis C virus. Bioorg Med Chem Lett. 2010 Aug 15; 20(16): 4850-4.

[3]. Li W, et, al. In Vitro Metabolite Formation in Human Hepatocytes and Cardiomyocytes and Metabolism and Tissue Distribution in Monkeys of the 2'-C-Methylguanosine Prodrug BMS-986094. Int J Toxicol. 2017 Jan 1; 1091581816683642.

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