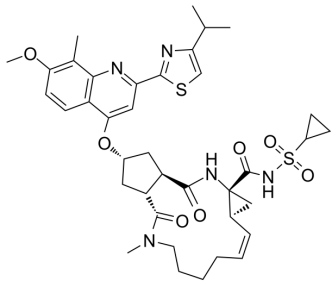
Simeprevir

Cat. No.:	HY-10241
CAS No.:	923604-59-5
Molecular Formula:	$C_{38}H_{47}N_5O_7S_2$
Molecular Weight:	749.94
Target:	HCV; HCV Protease; SARS-CoV; DNA/RNA Synthesis
Pathway:	Anti-infection; Metabolic Enzyme/Protease; Cell Cycle/DNA Damage
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 1 year -20°C 6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : 14.29 mg/mL (19.05 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.3334 mL	6.6672 mL	13.3344 mL
	5 mM	0.2667 mL	1.3334 mL	2.6669 mL
	10 mM	0.1333 mL	0.6667 mL	1.3334 mL

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

In Vivo

1. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: 2.5 mg/mL (3.33 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.43 mg/mL (1.91 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.43 mg/mL (1.91 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Simeprevir (TMC435; TMC435350) is an oral, potent and highly specific hepatitis C virus (HCV) NS3/4A protease inhibitor with a K_i of 0.36 nM. Simeprevir inhibits HCV replication with an EC_{50} of 7.8 nM. Simeprevir also potently suppresses SARS-CoV-2 replication and synergizes with Remdesivir. Simeprevir inhibits the main protease (M^{pro}) and the RNA-dependent RNA polymerase (RdRp) of SARS-CoV-2, and also modulates host immune responses[1][4].

IC_{50} & Target

K_i: 0.36 nM (HCV NS3/4A protease)[1]
EC_{50}: 7.8 nM (HCV replication)[1]

	IC_{50}: 9.6±2.3 μM (SARS-CoV-2 M^{pro}), 5.5±0.2 μM (SARS-CoV-2 RdRp)[4]
In Vitro	Simeprevir (TMC435) inhibits HCV in a dose-dependent manner in Huh7-Luc cells, with EC_{50} and EC_{90} values of 8 nM and 24 nM, respectively[2]. Simeprevir (TMC435) inhibits NS3/4A proteases from HCV genotypes 1 to 6 with IC_{50}s of 1/0.9/7/30/1.5/2.2/1.6 nM for 1a/1b/2b/3a/4/5/6, respectively[3]. Simeprevir inhibits SARS-CoV-2 in Vero E6 cells with IC_{50}s of 9.6±2.3 μM and 5.5±0.2 μM for M^{pro} and RdRp, respectively[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Simeprevir (TMC435) has moderate terminal elimination half-life ($t_{1/2}$=1.5 h and 4.1 h for rat (3 mg/kg, p.o.), monkey (3 mg/kg, p.o.))[3]. Simeprevir (TMC435350) exhibits a medium-slow rate of absorption, well distribution with the high concentration observed in the liver, and a low clearance[1]. Pharmacokinetic Parameters of Simeprevir (TMC435350) in male Sprague-Dawley rats[1].

	IV (2 mg/kg)	PO (10 mg/kg)
CL (L/h/kg)	0.505	
Vd_{ss} (h)	0.49	
AUC_{0-24} (μM·h)	5.21	2.79
C_{max} (μM)		0.73
T_{max} (h)		3.0
$T_{1/2}$ (h)		2.8
F (%)		11
Liver/plasma ratio at 6 h	63.5	32

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Animal Model:	Sprague-Dawley (SD) rats and cynomolgus monkeys[3]
Dosage:	3 mg/kg
Administration:	Oral administration
Result:	Time at which peak concentration (T_{max}) of 1 hour and 2 hour for rat and monkey, respectively. Concentration at 24 h after dosing ($C_{24\ h}$) of 0.9 and 2.3 ng/mL for rat and monkey, respectively. AUC_{0-24h}=1173 and1409 ng • h/mL for rat and monkey, respectively.

CUSTOMER VALIDATION

- Cancer Cell. 2022 Aug 26;S1535-6108(22)00372-5.
- Nat Methods. 2018 Jul;15(7):519-522.
- Cell Res. 2023 Sep 6.
- Signal Transduct Target Ther. 2021 May 29;6(1):212.
- Nat Commun. 2023 Nov 27;14(1):7753.

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REFERENCES

[1]. Lo HS, et al. Simeprevir Potently Suppresses SARS-CoV-2 Replication and Synergizes with Remdesivir. ACS Cent Sci. 2021 May 26;7(5):792-802.

[2]. Raboisson P, et al. Structure-activity relationship study on a novel series of cyclopentane-containing macrocyclic inhibitors of the hepatitis C virus NS3/4A protease leading to the discovery of TMC435350. Bioorg Med Chem Lett. 2008 Sep 1;18(17):4853-8.

[3]. Lin TI, et al. In vitro activity and preclinical profile of TMC435350, a potent hepatitis C virus protease inhibitor.Antimicrob Agents Chemother. 2009 Apr;53(4):1377-85. Epub 2009 Jan 26.

[4]. Rajagopalan R, et al. Preclinical Characterization and Human Microdose Pharmacokinetics of ITMN-8187, a Nonmacrocyclic Inhibitor of the Hepatitis C Virus NS3 Protease. Antimicrob Agents Chemother. 2016 Dec 27;61(1). pii: e01569-16.

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

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA