Simeprevir sodium

Cat. No.: HY-10241A

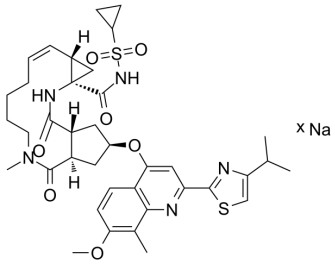
CAS No.: 1241946-89-3

Molecular Formula: $C_{38}H_{47}N_5NaO_7S_2$

Target: HCV; HCV Protease; SARS-CoV; DNA/RNA Synthesis

Pathway: Anti-infection; Metabolic Enzyme/Protease; Cell Cycle/DNA Damage

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Simeprevir (TMC435; TMC435350) sodium is an oral, potent and highly specific hepatitis C virus (HCV) NS3/4A protease inhibitor with a K_i of 0.36 nM. Simeprevir sodium inhibits HCV replication with an EC_{50} of 7.8 nM. Simeprevir sodium also potently suppresses SARS-CoV-2 replication and synergizes with Remdesivir. Simeprevir sodium 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 an IC_{50} 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

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

Animal Model:	Sprague-Dawley (SD) rats and cynomolgus monkeys[3]
Dosage:	3 mg/kg
Administration:	PO; single dosage
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. $AUC_{0\text{-}24h}$=1173 and 1409 ng·h/mL for rat and monkey, respectively.

CUSTOMER VALIDATION

- Nat Methods. 2018 Jul;15(7):519-522.
- Signal Transduct Target Ther. 2021 May 29;6(1):212.
- Nat Commun. 2020 Sep 4;11(1):4417.
- Proc Natl Acad Sci U S A. 2017 Feb 21;114(8):1922-1927.
- Acta Pharm Sin B. 2019 Jul;9(4):769-781.

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REFERENCES

[1]. 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.

[2]. 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.

[3]. 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.

[4]. 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.

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

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