

Product Data Sheet

Product Name: Narlaprevir

Cat. No.: GC14074

Chemical Properties

Cas. No. 865466-24-6

Chemical Name (1R,2S,5S)-3-[(2S)-2-[[1-(tert-butylsulfonylmethyl)cyclohexyl]carbamoylamino]-3,3-dimethylbutanoyl]-N-[(3S)-1-(cyclopropylamino)-1,2-dioxoheptan-3-yl]-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide

SMILES CCCCC(C(=O)C(=O)NC1CC1)NC(=O)C2C3C(C3(C)C)CN2C(=O)C(C(C)(C)C)NC(=O)NC4(CCCCC4)CS(=O)(=O)C(C)(C)C

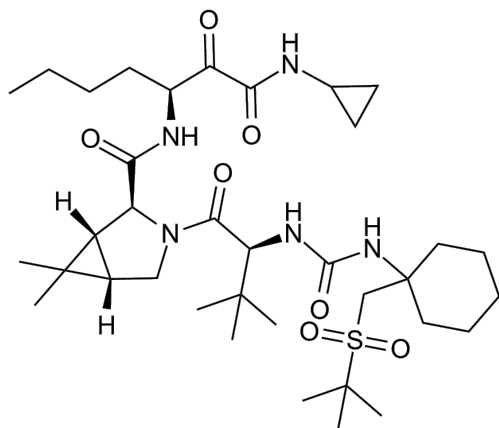
Formula C₃₆H₆₁N₅O₇S M.Wt 707.96

Solubility DMSO : ≥ 50 mg/mL (70.63 mM) Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

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

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Cell lines HCV replicon Huh-7 cells

Preparation Method Replicon cells were treated with Narlaprevir for 3 days, and replicon RNA levels were measured by TaqMan assay. The average (with SD) of the relative reduction in the replicon RNA level (dCT) from triplicate measurements was plotted against the log compound concentration.

Reaction
Conditions 72h

Applications The EC₅₀ and EC₉₀ values for Narlaprevir were 20 ± 6nM and 40 ± 10nM, respectively, in a 72h assay.

Animal experiment [2]:

Animal models Rat (strain and sex not specified)

Preparation Method Rats were given a single 10mg/kg oral dose of Narlaprevir. Blood samples were collected for pharmacokinetic analysis.

Dosage form 10mg/kg; p.o.

Applications A single oral dose of Narlaprevir (10mg/kg) demonstrated a bioavailability of 46% in rats, with a liver concentration of 750ng/g at 8h post-dose.

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References:

- [1] TONG X, ARASAPPAN A, BENNETT F, et al. Preclinical characterization of the antiviral activity of SCH 900518 (narlaprevir), a novel mechanism-based inhibitor of hepatitis C virus NS3 protease[J]. Antimicrobial Agents and Chemotherapy, 2010, 54(6): 2365-2370.
- [2] ARASAPPAN A, BENNETT F, BOGEN S L, et al. Discovery of narlaprevir (SCH 900518): a potent, second generation HCV NS3 serine protease inhibitor[J]. ACS Medicinal Chemistry Letters, 2010, 1(2): 64-69.

Background

Narlaprevir is a highly selective and orally active inhibitor of the hepatitis C virus non-structural protein 3 (HCV NS3), with a K_i value of 6nM and an EC_{50} value of 40nM^[1]. HCV NS3 plays a critical role in viral replication and possesses both protease and helicase functions^[2]. Narlaprevir inhibits viral replication in host cells by forming a reversible covalent bond with the active site of the HCV NS3 protease, and is commonly used in the treatment and research of chronic HCV infection^[3,4,5].

In vitro, treatment of HCV genotype 1b subgenomic replicon Huh-7 cells with Narlaprevir (EC_{50} = 20nM, EC_{90} = 40nM) for 72h significantly inhibited HCV RNA replication^[6].

In vivo, Narlaprevir (10mg/kg) was administered orally to rats, with a bioavailability of 46% and a liver concentration of 750ng/g 8h after administration^[1].

References:

- [1] ARASAPPAN A, BENNETT F, BOGEN S L, et al. Discovery of narlaprevir (SCH 900518): a potent, second generation HCV NS3 serine protease inhibitor[J]. ACS Medicinal Chemistry Letters, 2010, 1(2): 64-69.
- [2] ZHOU T, REN X, ADAMS R L, et al. NS3 from hepatitis C virus strain JFH-1 is an unusually robust helicase that is primed to bind and unwind viral RNA[J]. Journal of Virology, 2018, 92(1): e01253-17.
- [3] BAI Y, YE F, FENG Y, et al. Structural basis for the inhibition of the SARS-CoV-2 main protease by the anti-HCV drug narlaprevir[J]. Signal Transduction and Targeted Therapy, 2021, 6(1): 51.
- [4] ISAKOV V, KOLODA D, TIKHONOVA N, et al. Pharmacokinetics of the new hepatitis C virus NS3 protease inhibitor narlaprevir following single-dose use with or without ritonavir in patients with liver cirrhosis[J]. Antimicrobial Agents and Chemotherapy, 2016, 60(12): 7098-7104.

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[5] MARTINO S D, PETRI G L, DE ROSA M. Hepatitis C: the story of a long journey through first, second, and third generation NS3/4A peptidomimetic inhibitors. What did we learn?[J]. Journal of Medicinal Chemistry, 2024, 67(2): 885-921.

[6] TONG X, ARASAPPAN A, BENNETT F, et al. Preclinical characterization of the antiviral activity of SCH 900518 (narlaprevir), a novel mechanism-based inhibitor of hepatitis C virus NS3 protease[J]. Antimicrobial Agents and Chemotherapy, 2010, 54(6): 2365-2370.

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