Lomibuvir (VX-222)

Catalog No.C07831 Batch:C0783103

Product Datasheet

Technical Data

Formula	$C_{25}H_{35}NO_4S$					
Molecular Weight	445.61	**CAS No.**	1026785-59-0			
Solubility (25°C)*	In vitro	DMSO	89 mg/mL (199.72 mM)			
		Ethanol	89 mg/mL (199.72 mM)			
		Water	Insoluble			
	In vivo (Add solvents to the product individually and in order)	Oral Administration	Homogeneous suspension	CMC-NA	≥5mg/ml	Taking the 1 mL working solution as an example, add 5 mg of this product to 1 ml of CMC-Na solution, mix evenly to obtain a homogeneous suspension with a final concentration of 5 mg/ml.
		Injection	Clear solution	30%PEG400 [1]→ 0.5%Tween80 [2]→ 5%propylene glycol Validated by Capsid Bio labs. Should you need adjustments to this formulation, contact our sales team for custom testing.	30.000mg/ml (67.32mM)	Taking the 1 mL working solution as an example, add 300 μL of 100 mg/ml clarified PEG400 stock solution to 5 μL of Tween80, mix evenly to clarify it; add 50 μL Propylene glycol to the above system, mix evenly to clarify it; then continue to add 645 μL ddH2O to adjust the volume. to 1 mL. The mixed solution should be used immediately for optimal results.

* <1 mg/ml means slightly soluble or insoluble.
* Please note that Capsid Bio tests the solubility of all compounds in-house, and the actual solubility may differ slightly from published values. This is normal and is due to slight batch-to-batch variations.
* Room temperature shipping (Stability testing shows this product can be shipped at 2-8°C for storage purposes.)

Preparing Stock Solutions

Concentration \ Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.2441 mL	11.2206 mL	22.4411 mL
5 mM	0.4488 mL	2.2441 mL	4.4882 mL
10 mM	0.2244 mL	1.1221 mL	2.2441 mL
50 mM	0.0449 mL	0.2244 mL	0.4488 mL

Biological Activity

Description	Lomibuvir (VX-222, VCH-222) is a novel, potent and selective inhibitor of **HCV** polymerase with **IC50** of 0.94-1.2 μM. This compound is 15.3-fold less effective for mutant M423T, and 108-fold less effective for mutant I482L. Phase 2.
Targets	HCV NS5B 1a [1] : 0.94 μM HCV NS5B 1b [1] : 1.2 μM
In vitro	Lomibuvir (VX-222) binds to the thumb II allosteric pocket of the HCV RNA-dependent RNA polymerase. It exhibits non-competitive and selective inhibition in HCV NS5B of genotype 1a and 1b, with IC50 of 0.94 and 1.2 μM, respectively. This compound selectively inhibits the replication of subgenomic HCV genotype 1a and 1b with an EC50 of 22.3 and 11.2 nM, respectively. [1] Similarly, a recent study shows that it inhibits the 1b/Con1 HCV subgenomic replicon, with an EC50 of 5 nM. VX-222 preferentially inhibits primer-dependent RNA synthesis, showing only a modest or no effect on de novo-initiated RNA synthesis. [2]
In vivo	Lomibuvir (VX-222) displays a fine pharmacokinetic profile in rats and dogs, including low total body clearance and excellent oral bioavailability (greater than 30%) with good ADME properties. It is biotransformed by several enzymes (CYP1A1, 2A6, 2B6, 2C8, CYP 3A4, UGT1A3) and is predicted to be actively transported in the liver and excreted mainly intact in bile or as glucuronide adducts. [3]
Features	A novel, potent and selective inhibitor of non-nucleoside polymerase, specifically the HCV RNA-dependent RNA polymerase.

Protocol (from reference)

Kinase Assay:[1]

- **Anti-NS5B activity assay**

  The inhibitory effect of Lomibuvir (VX-222) on HCV NS5B activity is measured by evaluating the amount of radiolabeled UTP incorporated by the C-terminal Δ21 truncated version of enzyme in a newly synthesized RNA using a homopolymeric RNA template / primer namely poly rA / oligo dT. Quantitative detection of incorporated radioactivity is done using a liquid scintillation counter. The in vitro kinetics of inhibition of HCV NS5B from genotype 1b strain BK by this compound are determined using the C-terminal Δ21 truncated version of NS5B. It (1 to 1.5 μM) is tested in the presence of 10 to 75 μM nonradioactive UTP mixed with 0.89 to 6.70 μCi of [α-^{33}P]-labeled UTP. RNA-dependent-RNA polymerase reactions are allowed to proceed for 18 min at 22 °C.

Cell Assay:[2]

- **Cell lines**

  Huh7.5 cells
- **Concentrations**

  0.01 nM -10 μM
- **Incubation Time**

  48 hours

- **Method**

  Huh7.5 cells harboring HCV RNA replicons are trypsinized and plated into 48-well plates at a concentration of 4 × 10^4 cells/well. The next day the medium is changed and Lomibuvir (VX-222) is added in 200 μL of complete medium. After 48 hours, total RNA is extracted and viral RNAs are quantified by real-time reverse transcription-PCR (RT-PCR). The effective drug concentrations that reduced HCV RNA replicon levels by 50% (EC50) are calculated by nonlinear regression analysis with log curve fitting.

Animal Study:[3]

- **Animal Models**

  Rats or dogs
- **Dosages**

  5 mg/kg for rats or 10 mg/kg for dogs
- **Administration**

  By oral gavage

References

http://download.journals.elsevierhealth.com/pdfs/journals/0168-… https://pubmed.ncbi.nlm.nih.gov/22143520/ http://download.journals.elsevierhealth.com/pdfs/journals/0168-8…

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EU Headquarters
Gajeva ulica 28, HR-10000 Zagreb, Croatia

US Headquarters
12222 Merit Dr STE 130 Dallas, Texas, 75251

UK Headquarters
121 ABILITY HOUSE, BROOKER ROAD, EN9 1JH, ESSEX

Orders: Sales@capsidbio.com
Enquiries: info@capsidbio.com
www.capsidbio.com