Product Datasheet

Technical Data

Formula	$C_{17}H_{18}N_4O_2$					
Molecular Weight	310.35	**CAS No.**	473921-12-9			
Solubility (25°C)*	In vitro	DMSO	31 mg/mL (99.88 mM)			
		Ethanol	16 mg/mL (51.55 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	5%DMSO →[1] 40%PEG300 →[2] 5%Tween80 →[3] 50%ddH2O Validated by Capsid Bio labs. Should you need adjustments to this formulation, contact our sales team for custom testing.	1.550mg/ml (4.99mM)	Taking the 1 mL working solution as an example, add 50 μL of 31 mg/ml clarified DMSO stock solution to 400 μL PEG300, mix evenly to clarify it; add 50 μL Tween80 to the above system, mix evenly to clarify it; then continue to add 500 μL ddH2O to adjust the volume to 1 mL. The mixed solution should be used immediately for optimal results.
			Clear solution	5% DMSO →[1] 95% corn oil Validated by Capsid Bio labs. Should you need adjustments to this formulation, contact our sales team for custom testing.	1.550mg/ml (4.99mM)	Taking the 1 mL working solution as an example, add 50 μL of 31 mg/ml clear DMSO stock solution to 950 μL of corn oil and mix evenly. 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	3.2222 mL	16.1108 mL	32.2217 mL
5 mM	0.6444 mL	3.2222 mL	6.4443 mL
10 mM	0.3222 mL	1.6111 mL	3.2222 mL
50 mM	0.0644 mL	0.3222 mL	0.6444 mL

Biological Activity

Description	Lersivirine (UK-453061) is a potent and selective inhibitor of **nonnucleoside reverse transcriptase** (NNRTI) with **IC50** of 0.119 μM.
Targets	NNRT [2]
In vitro	Lersivirine (UK-453061) binds to HIV-1 wt reverse transcriptase (RT) with K_d of 624 nM. It is a very weak inhibitor of human DNA polymerase beta, with an extrapolated geometric mean IC50 of approximately 20 mM resulting in a predicted selectivity index of 166,000. This compound is able to inhibit HIV-1 virus replication in MT-2 cells infected with wt NL4-3, with an EC50 ranging from 5 nM to 35 nM against an MOI ranging from 0.005 to 0.5. It retains activity against 80% of viruses with genotypes containing K103N as a single NNRTI mutation (versus 7% for efavirenz), 57% of viruses with genotypes containing Y181C as a single NNRTI mutation (43% for efavirenz), and 46% of viruses with genotypes containing G190A as a single NNRTI mutation (0% for efavirenz). Lersivirine inhibits the replication of strain Ba-L in PBL, with a geometric mean EC50 equal to 3.38 nM (95% CI, 2.26 to 5.05 nM) and an EC90 equal to 9.87 nM (95% CI, 6.63 to 14.7 nM), with no cytotoxicity observed up to 50 μM. Combinations of it with drugs of the NRTI class (abacavir, didanosine, emtricitabine, lamivudine, tenofovir, and zidovudine) results in synergistic interactions. [1]
In vivo	In mice, Lersivirine (UK-453061) is not teratogenic.[3]

Protocol (from reference)

Kinase Assay:[1]

- **RT enzyme assays**
  The activities of lersivirine (UK-453061) and efavirenz against wt RT (BH10 strain) are determined using a primer extension assay incorporating a DNA/RNA primer/template. The 5'biotinylated primer DNA is a 16mer oligo(dT), which is annealed to a poly(rA) template of approximately 300 bases in length. Incorporation of [^{3}H]TTP(dTTP) by reverse transcription results in extension of the primer. During the reaction the primer/template is bound to a streptavidin-coated flashplate (NEN). The incorporated tritiated nucleotides can then stimulate the scintillant to produce a signal that is measured using a scintillation counter. Compounds that inhibit the RNA-dependent DNA polymerase activity of RT produce a reduced signal.

Cell Assay:[1]

- **Cell lines**
  SupT1 cells
- **Concentrations**
  increasing concentrations from 5 nM

- **Incubation Time**
  Every 7 days
- **Method**
  For inhibitor escalation studies, SupT1 cells are initially infected with HIV-1 NL4-3 wt for 1 h at 37°C and the virus-infected cells are passaged weekly in SupT1 cells in the presence of increasing concentrations of lersivirine (UK-453061) from a starting concentration of 5 nM (IC50 in this assay system) in 12-well plates (6×10^5 cells/well). Throughout the passaging period, ongoing virus replication is monitored weekly by observing cytopathic effects (syncytia). Every 7 days, virus supernatant is passaged onto fresh cells at the same density with fresh medium containing this compound. The concentration of it is increased by 2-fold and 5-fold that of the previous concentration upon subsequent passage whenever evidence of viral replication is observed. Virus stocks for phenotypic characterization are produced in SupT1 cells in the absence of compound and are tested for their sensitivity to lersivirine in an antiviral assay using HeLaP4 cells.

Animal Study:[3]

- **Animal Models**
  Mated Crl:CD1(ICR) mice
- **Dosages**
  150 mg/kg, 350 mg/kg, 500 mg/kg
- **Administration**
  Oral gavage

References

https://pubmed.ncbi.nlm.nih.gov/20660667/

https://pubmed.ncbi.nlm.nih.gov/19748778/

https://pubmed.ncbi.nlm.nih.gov/22447726/

RETURN POLICY

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SHIPPING & STORAGE

Capsid Bio products are transported at room temperature. If you receive the product at room temperature, please rest assured, the Capsid Bio Quality Inspection Department has conducted experiments to verify that the normal temperature placement of one month will not affect the biological activity of powder products. After collecting, please store the product according to the requirements described in the datasheet. Most Capsid Bio products are stable under the recommended conditions.

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