NVP-LCQ195

Cat. No.: HY-15241

CAS No.: 902156-99-4

Molecular Formula: $C_{17}H_{19}Cl_2N_5O_4S$

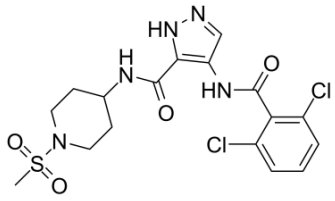
Molecular Weight: 460.33

Target: CDK

Pathway: Cell Cycle/DNA Damage

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (217.24 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	2.1724 mL	10.8618 mL	21.7235 mL
5 mM	0.4345 mL	2.1724 mL	4.3447 mL
10 mM	0.2172 mL	1.0862 mL	2.1724 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.43 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.43 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

NVP-LCQ195 (AT9311; LCQ195) is a small molecule heterocyclic inhibitor of CDK1, CDK2, CDK3 and CDK5 with IC50 of 1-42 nM.IC50 Value: 1 nM(CDK5/p25 and CDK5/p35); 2 nM(CDK1/cyclinB and CDK2/cyclinA); 5 nM(CDK2/cyclinE); 42 nM(CDK3/cyclinE)Target: CDKsLCQ195 induced cell cycle arrest and eventual apoptotic cell death of MM cells, even at sub-lmol/l concentrations, spared non-malignant cells, and overcame the protection conferred to MM cells by stroma or cytokines of the bone marrow milieu. In MM cells, LCQ195 triggered decreased amplitude of transcriptional signatures associated with oncogenesis, drug resistance and stem cell renewal, including signatures of activation of key transcription factors for MM cells e.g. myc, HIF-1a, IRF4. Bortezomib-treated MM patients whose tumours had high baseline expression of genes suppressed byLCQ195 had significantly shorter progression-free and overall survival than those with low levels of

	these transcripts in their MM cells. These observations provide insight into the biological relevance of multi-targeted CDK inhibition in MM.

IC_{50} & Target	Cdk5/p25 1 nM (IC_{50})	CDK5/p35 1 nM (IC_{50})	Cdk1/cyclin B 2 nM (IC_{50})	cdk2/cyclin A 2 nM (IC_{50})
	CDK2/cyclinE 5 nM (IC_{50})	CDK9/cyclinT1 15 nM (IC_{50})	CDK3/Cyclin E 42 nM (IC_{50})	cdk6/cyclin D3 187 nM (IC_{50})
	CDK7/Cyclin H/MAT1 3564 nM (IC_{50})			

REFERENCES

[1]. McMillin DW, Delmore J, Negri J et al. Molecular and cellular effects of multi-targeted cyclin-dependent kinase inhibition in myeloma: biological and clinical implications. Br J Haematol. 2011 Feb;152(4):420-32.

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