Voruciclib hydrochloride

Cat. No.: HY-12422A

CAS No.: 1000023-05-1

Molecular Formula: $C_{22}H_{20}Cl_2F_3NO_5$

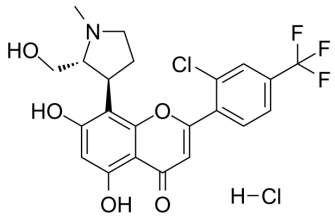
Molecular Weight: 506.3

Target: CDK

Pathway: Cell Cycle/DNA Damage

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 250 mg/mL (493.78 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.9751 mL	9.8756 mL	19.7511 mL
5 mM	0.3950 mL	1.9751 mL	3.9502 mL
10 mM	0.1975 mL	0.9876 mL	1.9751 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: ≥ 2.08 mg/mL (4.11 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.11 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.11 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Voruciclib hydrochloride is an orally active and selective CDK inhibitor with K_i values of 0.626 nM-9.1 nM. Voruciclib hydrochloride potently blocks CDK9, the transcriptional regulator of MCL-1. Voruciclib hydrochloride represses expression of MCL-1 in multiple models of diffuse large B-cell lymphoma (DLBCL)[1].

IC_{50} & Target

CDK9/CycT1 1.68 nM (Ki)	CDK9/cyc T2 0.626 nM (Ki)	CDK6/cycD1 2.92 nM (Ki)	CDK4/Cyc D1 3.96 nM (Ki)
CDK1/cycB	CDK1/cyc A		

	5.4 nM (Ki)	9.1 nM (Ki)

In Vitro

Voruciclib hydrochloride (0.5-5 μM; 6 hours) shows targeted downregulation of MCL-1 in both ABC and GCB subtypes[1].
K_i values for each target such as CDK9/cyc T2, CDK9/cyc T1, CDK6/cyc D1, CDK4/cyc D1, CDK1/cyc B, and CDK1/cyc A for Voruciclib hydrochloride are 0.626 nM, 1.68 nM, 2.92 nM, 3.96 nM, 5.4 nM, 9.1 nM, respectively[1].

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

Western Blot Analysis[1]

Cell Line:	U2932, RIVA, OCI-LY10 cells (ABC subtype), NU-DHL-1, SU-DHL-4, SU-DHL-6 cells (GCB subtype)
Concentration:	0.5 μM, 1 μM, 2 μM, 3 μM, 4 μM, 5 μM
Incubation Time:	6 hours
Result:	Showed targeted downregulation of MCL-1 in both ABC and GCB subtypes.

In Vivo

Combination of Voruciclib hydrochloride (200 mpk; Oral gavage) and Venetoclax (10 mpk, 1 mpk, 50 mpk, 25 mpk in U2932, RIVA, SU-DHL-4 and NU-DHL-1, respectively) leads to enhance tumor growth inhibition compared to either drug alone in U2932, RIVA, SU-DHL-4 (six days per week for 4 weeks), and NU-DHL-1 models (five days per week for 3 weeks) of DLBCL[1].

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

Animal Model:	ABC subtypes (U2932, RIVA, OCI-LY10), GCB subtypes (SU-DHL-4, NU-DHL-1) xenografted in Female NOD.CB17-Prkdcscid/NCrHsd mice[1]
Dosage:	200 mpk
Administration:	Oral gavage; U2932, RIVA, SU-DHL-4 (six days per week for 4 weeks), OCI-LY10 (six days per week for 2 weeks), NU-DHL-1 (five days per week for 3 weeks)
Result:	Enhanced tumor growth inhibition in U2932, RIVA, SU-DHL-4 and NU-DHL-1 models except in OCI-LY10 model.

REFERENCES

[1]. Dey J, et al. Voruciclib, a clinical stage oral CDK9 inhibitor, represses MCL-1 and sensitizes high-risk Diffuse Large B-cell Lymphoma to BCL2 inhibition. Sci Rep. 2017 Dec 21;7(1):18007.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA