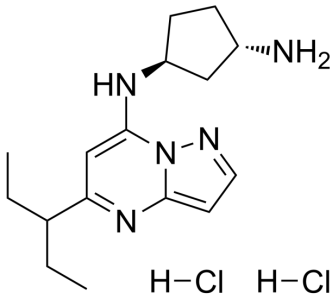
KB-0742 dihydrochloride

Cat. No.:	HY-137478A
CAS No.:	2416874-75-2
Molecular Formula:	$C_{16}H_{27}Cl_2N_5$
Molecular Weight:	360.33
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

H_2O : 100 mg/mL (277.52 mM; Need ultrasonic)
DMSO : 62.5 mg/mL (173.45 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.7752 mL	13.8762 mL	27.7523 mL
5 mM	0.5550 mL	2.7752 mL	5.5505 mL
10 mM	0.2775 mL	1.3876 mL	2.7752 mL

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

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 100 mg/mL (277.52 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (5.77 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.77 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.77 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

KB-0742 dihydrochloride is a potent, selective and orally active CDK9 inhibitor with an IC_{50} of 6 nM for CDK9/cyclin T1. KB-0742 dihydrochloride is selective for CDK9/cyclin T1 with >50-fold selectivity over other CDK kinases. KB-0742 dihydrochloride has potent anti-tumor activity[1].

IC_{50} & Target

CDK9/cyclinT1
6 nM (IC_{50})

In Vitro

KB-0742 (6 hours; 0.1-10 μM; 22Rv1 cells) treatment significant reduction of downstream phosphorylation of RNA Pol II at Ser2 and Ser7, and diminished phosphorylation at Ser5. Global androgen receptor (AR)-FL and AR-V protein levels are significantly reduced starting at 6 h treatment time, which is accompanied by the reduction of phospho-AR levels (Ser81)[1].
KB-0742 (48-72 hours) treatment shows cytostatic effects in prostate cancer and leukemia cell lines. KB-0742 shows antiproliferative activity with GR_{50}s of 0.183 μM and 0.288 μM for 22Rv1 cells and MV-4-11 AML cells, respectively[1].
In 22Rv1 cells, KB-0742 rapidly downregulates nascent transcription, preferentially depleting short half-life transcripts and AR-driven oncogenic programs[1].

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

Western Blot Analysis[1]

Cell Line:	22Rv1 cells
Concentration:	0.1 μM, 0.5 μM, 1 μM, 10 μM
Incubation Time:	6 hours
Result:	Significant reduction of downstream phosphorylation of RNA Pol II at Ser2 and Ser7, and diminished phosphorylation at Ser5.

In Vivo

KB-0742 (3-30 mg/kg; p.o.; daily; over 21 days) is well tolerated even at high dose, while significantly reducing tumor burden in 22Rv1 human prostate cancer cell line-derived xenograft (CDX) models[1].

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

Animal Model:	Male CB17-SCID mice injected with 22Rv1 human prostate cancer cells[1]
Dosage:	3 mg/kg, 10 mg/kg, and 30 mg/kg
Administration:	p.o.; daily; over 21 days
Result:	Significantly reduced tumor growth in castration-resistant prostate cancer (CRPC).

REFERENCES

[1]. André Richters, et al. Modulating Androgen Receptor-Driven Transcription in Prostate Cancer with Selective CDK9 Inhibitors. Cell Chem Biol. 2020 Oct 20;S2451-9456(20)30380-9.

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