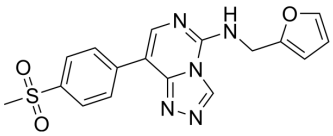
EED226

Cat. No.:	HY-101117
CAS No.:	2083627-02-3
Molecular Formula:	$C_{17}H_{15}N_5O_3S$
Molecular Weight:	369.4
Target:	Histone Methyltransferase
Pathway:	Epigenetics
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 125 mg/mL (338.39 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.7071 mL	13.5355 mL	27.0709 mL
	5 mM	0.5414 mL	2.7071 mL	5.4142 mL
	10 mM	0.2707 mL	1.3535 mL	2.7071 mL

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

In Vivo

1. Add each solvent one by one: 0.5%HPMC >> 1%Tween80
   Solubility: 10 mg/mL (27.07 mM); Suspened solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.77 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.77 mM); Suspended solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.77 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

EED226 is a polycomb repressive complex 2 (PRC2) inhibitor, which binds to the K27me3-pocket on embryonic ectoderm development (EED) and shows strong antitumor activity in xenograft mice model[1]. EED226 is a potent, selective, and orally bioavailable EED inhibitor[2]. EED226 inhibits PRC2 with an IC_{50} of 23.4 nM when the H3K27me0 peptide is used as a substrate in the in vitro enzymatic assays[3].

IC_{50} & Target	IC50: 23.4 nM (PRC2)[3]
In Vitro	EED226 is a highly potent, efficient and selective inhibitor of EZH2 and EZH1 evaluated against a broad range of epigenetic and non-epigenetic targets. It potently reduces global H3K27Me3 mark in cells and demonstrates selectively cell killing effects in cells carrying a heterozygous Y641N mutation. EED226 has moderate permeability as the measured in Caco-2 cells at A→B=3.0x10^{-6} cm/s, with an efflux ratio at 7.6[2]. In the in vitro enzymatic assays, EED226 inhibited PRC2 with an IC_{50} of 53.5 nM when the mononucleosome is used as the substrate, with the stimulatory H3K27me3 added at 1× K_{act} (1.0 μM)[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	EED226 induces robust and sustained tumor regression in $EZH2^{MUT}$ pre-clinical DLBCL model. In CD-1 mice, dosing of EED226 for 14 days at 300 mg/kg bid is well tolerated with no apparent adverse effects. It has very low in vivo clearance, and approximately 100% oral bioavailability. EED226 has low volume of distribution (0.8 L/kg), reasonable terminal $t_{1/2}$ (2.2 h), and moderate plasma protein binding (PPB)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2]	Mice: EED226 is formulated as a suspension in 0.5% PHMC+0.5% Tween 80 in water and administered orally by gavage at a dose volume of 10 mL/kg to the tumor bearing mice. At the end point, the animals is given the first dose administration. For PK analysis 100 μL of blood samples are collected from each animal by orbital sinus bleeding. For analysis of compound levels and PD in tissues, tumors are collected 4 hr post treatment and frozen immediately in liquid nitrogen. Tumor and body weight change data are analyzed statistically[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Chem Biol. 2023 Mar 27.
- Genome Biol. 2020 Aug 6;21(1):195.
- Cell Death Dis. 2022 Feb 15;13(2):155.
- iScience. 2023 May 31.
- ACS Infect Dis. 2020 Jul 10;6(7):1719-1733.

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REFERENCES

[1]. Huang Y, et al. Discovery of First-in-Class, Potent, and Orally Bioavailable Embryonic Ectoderm Development (EED) Inhibitor with Robust Anticancer Efficacy. J Med Chem. 2017 Mar 23;60(6):2215-2226.

[2]. Li L, et al. Discovery and Molecular Basis of a Diverse Set of Polycomb Repressive Complex 2 Inhibitors Recognition by EED. PLoS One. 2017 Jan 10;12(1):e0169855.

[3]. Qi W, et al. An allosteric PRC2 inhibitor targeting the H3K27me3 binding pocket of EED. Nat Chem Biol. 2017 Apr;13(4):381-388.

Caution: Product has not been fully validated for medical applications. For research use only.

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