Tazemetostat

Cat. No.: HY-13803

CAS No.: 1403254-99-8

Molecular Formula: $C_{34}H_{44}N_4O_4$

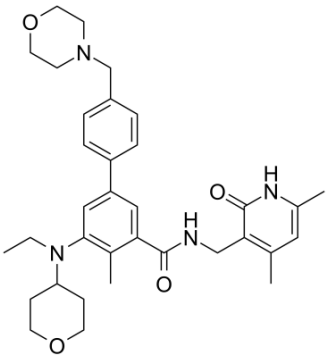
Molecular Weight: 572.74

Target: Histone Methyltransferase

Pathway: Epigenetics

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 : ≥ 25 mg/mL (43.65 mM)

0.1 M HCL : 14.29 mg/mL (24.95 mM; ultrasonic and adjust pH to 5 with HCl)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	1.7460 mL	8.7300 mL	17.4599 mL
5 mM	0.3492 mL	1.7460 mL	3.4920 mL
10 mM	0.1746 mL	0.8730 mL	1.7460 mL

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

In Vivo

1. Add each solvent one by one: 0.5% CMC-Na >> 0.1% Tween-80
   Solubility: 50 mg/mL (87.30 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (4.36 mM); Clear solution
3. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.36 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (3.63 mM); Clear solution
5. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.63 mM); Clear solution
6. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.63 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	Tazemetostat (EPZ-6438) is a potent, selective and orally available EZH2 inhibitor. Tazemetostat (EPZ-6438) inhibits the activity of human polycomb repressive complex 2 (PRC2)-containing wild-type EZH2 with a K_i value of 2.5 nM. Tazemetostat (EPZ-6438) inhibits EZH2 with IC_{50}s of 11 and 16 nM in peptide assay and nucleosome assay, respectively. Tazemetostat (EPZ-6438) inhibits rat EZH2 with an IC_{50} of 4 nM. Tazemetostat (EPZ-6438) also inhibits EZH1 with an IC_{50} of 392 nM[1].

IC_{50} & Target			
EZH2 WT 2.5 nM (Ki)	EZH2 11 nM (IC_{50}, in peptide assay)	EZH2 16 nM (IC_{50}, in nucleosome assay)	Rat EZH2 4 nM (IC_{50})
EZH1 392 nM (IC_{50})			

In Vitro

Tazemetostat (EPZ-6438) inhibits multi wild-type and mutant lymphoma cell lines proliferation with IC_{50}s of 0.49 nM-7.6 μM [1].

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

Cell Proliferation Assay[1]

Cell Line:	Wild-type and mutant lymphoma cell lines: DOHH-2 cell (EZH2 wild-type), Farage cell (EZH2 wild-type), OCI-LY19 cell (EZH2 wild-type), Toledo cell (EZH2 wild-type), KARPAS-422 (EZH2 Y646N), Pfeiffer (EZH2 A682G), RL cell line (EZH2 Y646N), SU-DHL-10 (EZH2 Y646F), SU-DHL-6 (EZH2 Y646N), WSU-DLCL2 (EZH2 Y646F)
Concentration:	0.49 nM-7.6 μM
Incubation Time:	11 days
Result:	Inhibited DOHH-2 cell (EZH2 wild-type; IC_{50}=1.7 μM), Farage cell (EZH2 wild-type; IC_{50}=99 nM), OCI-LY19 cell (EZH2 wild-type; IC_{50}=6.2 μM), Toledo cell (EZH2 wild-type; IC_{50}=7.6 μM), KARPAS-422 (EZH2 Y646N; IC_{50}=1.8 nM), Pfeiffer (EZH2 A682G; IC_{50}=0.49 nM), RL cell line (EZH2 Y646N; IC_{50}=5.8 μM), SU-DHL-10 (EZH2 Y646F; IC_{50}=5.8 nM), SU-DHL-6 (EZH2 Y646N; IC_{50}=4.7 nM), WSU-DLCL2 (EZH2 Y646F; IC_{50}=8.6 nM) proliferation.

In Vivo

Tazemetostat (EPZ-6438; 250 or 500 mg/kg twice daily for 21-28 days) practically eliminates the fast-growing G401 tumors[1].

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

Animal Model:	SCID mice bearing s.c. G401 xenografts[1]
Dosage:	125 mg/kg, 250 mg/kg, 500 mg/kg
Administration:	Oral; twice daily; 28 days
Result:	Practically eliminated the fast-growing G401 tumors at 250 or 500 mg/kg.

CUSTOMER VALIDATION

- Nat Med. 2017 Nov;23(11):1352-1361.
- Nat Commun. 2019 Jul 1;10(1):2901.
- Nat Struct Mol Biol. 2018 Mar;25(3):225-232.
- J Clin Invest. 2018 Jan 2;128(1):483-499.
- Cancer Res. 2019 Oct 1;79(19):4814-4827.

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REFERENCES

[1]. Knutson SK, et al. Durable tumor regression in genetically altered malignant rhabdoid tumors by inhibition of methyltransferaseEZH2. Proc Natl Acad Sci U S A. 2013 May 7;110(19):7922-7.

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