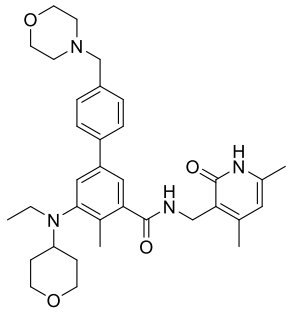
Product data sheet

MedKoo Cat#: 406265 Name: Tazemetostat CAS#: 1403254-99-8 (free base) Chemical Formula: $C_{34}H_{44}N_4O_4$ Exact Mass: 572.33626 Molecular Weight: 572.74	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

Tazemetostat, also known as EPZ-6438 and E7438, is a potent, selective, and orally bioavailable small-molecule inhibitor of EZH2 enzymatic activity. EPZ-6438 induces apoptosis and differentiation specifically in SMARCB1-deleted MRT cells. Treatment of xenograft-bearing mice with EPZ-6438 leads to dose-dependent regression of MRTs with correlative diminution of intratumoral trimethylation levels of lysine 27 on histone H3, and prevention of tumor regrowth after dosing cessation. These data demonstrate the dependency of SMARCB1 mutant MRTs on EZH2 enzymatic activity and portend the utility of EZH2-targeted drugs for the treatment of these genetically defined cancers.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	62.5	109.12

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.75 mL	8.73 mL	17.46 mL
5 mM	0.35 mL	1.75 mL	3.49 mL
10 mM	0.17 mL	0.87 mL	1.75 mL
50 mM	0.03 mL	0.17 mL	0.35 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Zhang H, Zhu D, Zhang Z, Kaluz S, Yu B, Devi NS, Olson JJ, Van Meir EG. EZH2 targeting reduces medulloblastoma growth through epigenetic reactivation of the BAI1/p53 tumor suppressor pathway. Oncogene. 2020 Jan;39(5):1041-1048. doi: 10.1038/s41388-019-1036-7. Epub 2019 Oct 3. Erratum in: Oncogene. 2019 Nov 1;: PMID: 31582835; PMCID: PMC7780546.
2. Kawano S, Grassian AR, Tsuda M, Knutson SK, Warholic NM, Kuznetsov G, Xu S, Xiao Y, Pollock RM, Smith JS, Kuntz KK, Ribich S, Minoshima Y, Matsui J, Copeland RA, Tanaka S, Keilhack H. Preclinical Evidence of Anti-Tumor Activity Induced by EZH2 Inhibition in Human Models of Synovial Sarcoma. PLoS One. 2016 Jul 8;11(7):e0158888. doi: 10.1371/journal.pone.0158888. Erratum in: PLoS One. 2017 Jan 13;12 (1):e0170539. PMID: 27391784; PMCID: PMC4938529.

In vivo study

1. Chan-Penebre E, Armstrong K, Drew A, Grassian AR, Feldman I, Knutson SK, Kuplast-Barr K, Roche M, Campbell J, Ho P, Copeland RA, Chesworth R, Smith JJ, Keilhack H, Ribich SA. Selective Killing of SMARCA2- and SMARCA4-deficient Small Cell Carcinoma of the Ovary, Hypercalcemic Type Cells by Inhibition of EZH2: In Vitro and In Vivo Preclinical Models. Mol Cancer Ther. 2017 May;16(5):850-860. doi: 10.1158/1535-7163.MCT-16-0678. Epub 2017 Mar 14. PMID: 28292935.

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2. Prokopuk L, Hogg K, Western PS. Pharmacological inhibition of EZH2 disrupts the female germline epigenome. Clin Epigenetics. 2018 Mar 5;10:33. doi: 10.1186/s13148-018-0465-4. PMID: 29515677; PMCID: PMC5836460.

7. Bioactivity

Biological target:

Tazemetostat (EPZ-6438) is a potent and selective EZH2 inhibitor.

In vitro activity

First, this study examined whether pharmacological inhibition of EZH2 had anti-tumor effects on MB cells in culture and found that treatment with EPZ-6438 greatly inhibited MB cell growth in vitro (Fig. 1a). To determine whether reduced cell growth was related to cell proliferation, this study performed cell cycle analysis and found a G0/G1 block (Fig. 1b and Suppl. Fig.1). As p53 is a major regulator of cell cycle progression, this study repeated the experiment in cells stably expressing TP53-shRNA and observed neutralization of EPZ-6438's inhibitory effect on MB cell growth (Fig. 1b, c). Since BAI1 can stabilize p53 by blocking Mdm2 and is silenced in MB cells, this studyfurther tested whether the growth inhibitory effect of EPZ-6438 is dependent upon reactivation of BAI1 tumor suppression activity and found ADGRB1-shRNAs indeed abrogated the anti-proliferative effect (Fig. 1d). Taken together, these results demonstrate that EPZ-6438 inhibits in vitro MB cancer cell growth in a BAI1/p53-dependent manner.

Reference: Oncogene. 2020 Jan; 39(5): 1041–1048. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7780546/

In vivo activity

This study investigated the potential for drugs that inhibit EZH2 to alter H3K27me3 in growing oocytes, primary oocytes and the developing female germline. Significantly, tazemetostat prevented H3K27me3 enrichment in growing oocytes of adult female mice in vivo, and this effect was relatively stable as H3K27me3 did not recover after 10 days of drug withdrawal. In addition, EZH2 inhibition reduced H3K27me3 in the primary oocyte pool, indicating that the lifelong primordial follicle reserve is affected by these drugs. Finally, tazemetostat severely depleted H3K27me3 in developing oocytes undergoing epigenetic reprogramming and established that once depleted, H3K27me3 did not recover in these cells within the window analysed. Combined, these findings demonstrate that EZH2 inhibitors potently reduce H3K27me3 at all stages of female germline development.

Reference: Clin Epigenetics. 2018; 10: 33. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5836460/