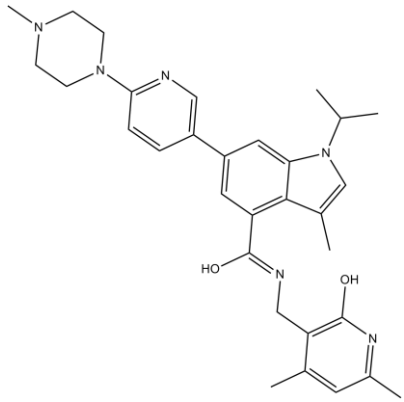
Product Data Sheet

Chemical Properties



Product Name:	GSK503
Cas No.:	1346572-63-1
M.Wt:	526.67
Formula:	C31H38N6O2
Synonyms:	N/A
Chemical Name:	(Z)-N-((2-hydroxy-4,6-dimethylpyridin-3-yl)methyl)-1-isopropyl-3-methyl-6-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)-1H-indole-4-carbimidic acid
Canonical SMILES:	CC(N(C1=CC(C2=CN=C(N3CCN(CC3)C)C=C2)=CC(/C(O)=N/CC4=C(O)N=C(C=C4C)C)=C51)C=C5C)C
Solubility:	≥21.65 mg/mL in DMSO, <2.7 mg/mL in H2O, ≥26.85 mg/mL in EtOH with gentle warming
Storage:	Store at -20°C
General tips:	For obtaining a higher solubility , please warm the tube at 37° C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20° C for several months.
Shopping Condition:	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request

Biological Activity

Targets :	Stem Cell
Pathways:	EZH2

Description:

GSK503 is a potent inhibitor of EZH2.
Enhancer of zeste homolog 2 (EZH2) is a histone-lysine N-methyltransferase enzyme that

catalyses trimethylation of lysine 27 in histone 3 (H3K27me3), and then induces chromatin compaction and consequently inhibits target genes transcription.
GSK503 is a potent EZH2 inhibitor with anticancer activity. In human melanoma cells, GSK503 significantly reduced H3K27me3 levels, induced G1 cell cycle arrest and slowed down cell growth [1].
In mice, GSK503 induced reversible weight loss by ~10%. In mice with skin melanomas, GSK503 reduced H3K27me3 levels in tumour and stromal cells, and significantly reduced the emergence of new skin melanomas. Also, GSK503 significantly inhibited the proliferation of tumour cells. In C57Bl/6 mice xenografted murine B16-F10 melanoma cells, GSK503 significantly reduced H3K27me3 levels and inhibited tumor growth. Also, GSK503 inhibited lymph node and lung metastases of melanoma and reduced lung nodule counts. GSK503 increased the expression of deoxycytidine kinase (DCK), adenosylmethionine decarboxylase 1 (AMD1) and WD repeat domain 19 (WDR19), which were EZH2 target genes [1].

***Reference**:*

[1]. Zingg D, Debbache J, Schaefer SM, et al. The epigenetic modifier EZH2 controls melanoma growth and metastasis through silencing of distinct tumour suppressors. Nat Commun, 2015, 6: 6051.

Protocol

Cell experiment:

Cell lines	Human melanoma cells
Preparation method	The solubility of this compound in DMSO is >21.65mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37 ℃ for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20℃ for several months.
Reacting conditions	
Applications	GSK503 significantly reduced H3K27me3 levels, induced G1 cell cycle arrest and slowed down cell growth.

Animal experiment [3]:

Animal models	Mice engrafted subcutaneously with melanoma cells, C57Bl/6 mice xenografted murine B16-F10 melanoma cells
Dosage form	Intraperitoneal injections; 150 mg/kg; 35 consecutive days
Applications	GSK503 treatment drastically reduced the emergence of new skin melanomas over time after treatment start. GSK503 treatment prevented murine melanoma growth. GSK503 significantly inhibited

	the proliferation of tumour cells. In C57Bl/6 mice xenografted murine B16-F10 melanoma cells, GSK503 significantly reduced H3K27me3 levels and inhibited tumor growth. GSK503 inhibited lymph node and lung metastases of melanoma and reduced lung nodule counts.
Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

***Reference**:*

[1]. Zingg D, Debbache J, Schaefer SM, et al. The epigenetic modifier EZH2 controls melanoma growth and metastasis through silencing of distinct tumour suppressors. Nat Commun, 2015, 6: 6051.

Product Citations

1. R.Martin Mateos, T.M.De Assuncao, et al. "Enhancer of Zeste Homologue 2 inhibition attenuates TGF-β dependent hepatic stellate cell activation and liver fibrosis." Cellular and Molecular Gastroenterology and Hepatology Available online 15 September 2018.
2. Sarmento OF, Svingen PA, et al. "The Role of the Histone Methyltransferase Enhancer of Zeste Homolog 2 (EZH2) in the Pathobiological Mechanisms Underlying Inflammatory Bowel Disease (IBD)." J Biol Chem. 2017 Jan 13;292(2):706-722. PMID:27909059

Caution

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.

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