

PRODUCT INFORMATION



EPZ015666

Item No. 17285

CAS Registry No.: 1616391-65-1
Formal Name: N-[(2S)-3-(3,4-dihydro-2(1H)-isoquinolinyl)-2-hydroxypropyl]-6-(3-oxetanyl-amino)-4-pyrimidinocarboxamide

Synonym: GSK3235025

MF: C₂₀H₂₅N₅O₃

FW: 383.4

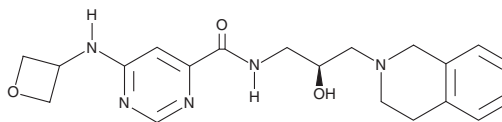
Purity: ≥95%

UV/Vis.: λ_{max}: 246, 304 nm

Supplied as: A crystalline solid

Storage: -20°C

Stability: ≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

EPZ015666 is supplied as a crystalline solid. A stock solution may be made by dissolving the EPZ015666 in the solvent of choice, which should be purged with an inert gas. EPZ015666 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of EPZ015666 in ethanol is approximately 10 mg/ml and approximately 30 mg/ml in DMSO and DMF.

EPZ015666 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, EPZ015666 should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. EPZ015666 has a solubility of approximately 0.5 mg/ml in a 1:1 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

Protein arginine methyltransferases (PRMTs) target nuclear and cytoplasmic substrates and can alter protein actions and gene expression.^{1,2} PRMT5, which can methylate histones H2A, H3, and H4, ribonucleoproteins, and other proteins, is upregulated in several human cancers, including lymphomas.³ Moreover, suppression of PRMT5 expression induces lymphoma cell death.⁴ EPZ015666 is a potent, orally bioavailable inhibitor of PRMT5 (K_i = 5 nM).⁵ It displays more than 20,000-fold selectivity for PRMT5 over other PMTs. EPZ015666 acts by blocking the association of PRMT5 with methylome protein 50, which is necessary for the formation of an active methyltransferase complex. EPZ015666 (100 mg/kg twice daily) blocks the growth of mantle cell lymphoma Z-138 xenografts, without significant body weight loss, in mice.⁵

References

1. Bissinger, E.-M., Heinke, R., Sippl, W., *et al.* Targeting epigenetic modifiers: Inhibitors of histone methyltransferases. *Med. Chem. Commun.* **1(2)**, (2010).
2. Copeland, R.A., Solomon, M.E., and Richon, V.M. Protein methyltransferases as a target class for drug discovery. *Nat. Rev. Drug Discov.* **8**, 724-732 (2009).
3. Li, Y., Chitnis, N., Nakagawa, H., *et al.* PRMT5 is required for lymphomagenesis triggered by multiple oncogenic drivers. *Cancer Discov.* **5**, 288-303 (2015).
4. Chung, J., Karkhanis, V., Tae, S., *et al.* Protein arginine methyltransferase 5 (PRMT5) inhibition induces lymphoma cell death through reactivation of the retinoblastoma tumor suppressor pathway and polycomb repressor complex 2 (PRC2) silencing. *J. Biol. Chem.* **288(49)**, 35534-35547 (2013).
5. Chan-Penebre, E., Kuplast, K.G., Majer, C.R., *et al.* A selective inhibitor of PRMT5 with *in vivo* and *in vitro* potency in MCL models. *Nat. Chem. Biol.* **11(6)**, 432-437 (2015).

WARNING

THIS PRODUCT IS FOR RESEARCH ONLY - NOT FOR HUMAN OR VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

SAFETY DATA

This material should be considered hazardous until further information becomes available. Do not ingest, inhale, get in eyes, on skin, or on clothing. Wash thoroughly after handling. Before use, the user must review the complete Safety Data Sheet, which has been sent via email to your institution.

WARRANTY AND LIMITATION OF REMEDY

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