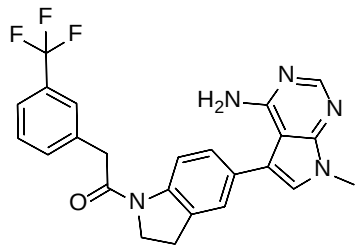
Product data sheet

MedKoo Cat#: 406393 Name: GSK2606414 CAS#: 1337531-36-8 Chemical Formula: $C_{24}H_{20}F_3N_5O$ Exact Mass: 451.1620 Molecular Weight: 451.44	
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:
GSK2606414 is an orally available, potent, and selective PERK inhibitor. GSK2606414 inhibits PERK activation in cells and inhibits the growth of a human tumor xenograft in mice. Protein kinase R (PKR)-like endoplasmic reticulum kinase (PERK) is activated in response to a variety of endoplasmic reticulum stresses implicated in numerous disease states. Evidence that PERK is implicated in tumorigenesis and cancer cell survival stimulated our search for small molecule inhibitors.

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
DMF	10.0	22.15
DMSO	55.38	122.67
DMSO:PBS (pH 7.2) (1:3)	0.25	0.55
Ethanol	11.5	25.47

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.22 mL	11.08 mL	22.15 mL
5 mM	0.44 mL	2.22 mL	4.43 mL
10 mM	0.22 mL	1.11 mL	2.22 mL
50 mM	0.04 mL	0.22 mL	0.44 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. Jiang X, Wei Y, Zhang T, Zhang Z, Qiu S, Zhou X, Zhang S. Effects of GSK2606414 on cell proliferation and endoplasmic reticulum stress-associated gene expression in retinal pigment epithelial cells. Mol Med Rep. 2017 May;15(5):3105-3110. doi: 10.3892/mmr.2017.6418. Epub 2017 Mar 30. PMID: 28358434.

In vivo study

1. Meng C, Zhang J, Dang B, Li H, Shen H, Li X, Wang Z. PERK Pathway Activation Promotes Intracerebral Hemorrhage Induced Secondary Brain Injury by Inducing Neuronal Apoptosis Both in Vivo and in Vitro. Front Neurosci. 2018 Feb 28;12:111. doi: 10.3389/fnins.2018.00111. PMID: 29541018; PMCID: PMC5835756.

7. Bioactivity
Biological target: GSK2606414 is a protein kinase R-like endoplasmic reticulum kinase (PERK) inhibitor with an IC50 of 0.4 nM.

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In vitro activity

The effects of GSK2606414 on proliferation, apoptosis, and the expression of activating transcription factor 4 (ATF4), CCAAT/enhancer-binding protein homologous protein (CHOP) and vascular endothelial growth factor (VEGF) in human retinal pigment epithelial (RPE) cells under endoplasmic reticulum (ER) stress were investigated. GSK2606414 treatment inhibited RPE cell proliferation in a dose-dependent manner, however it did not induce apoptosis. In addition, GSK2606414 treatment inhibited eIF2α phosphorylation and reduced CHOP and VEGF mRNA expression levels in RPE cells under TG (thapsigargin) induced ER stress.

Reference: Mol Med Rep. 2017 May;15(5):3105-3110. https://www.spandidos-publications.com/mmr/15/5/3105

In vivo activity

The roles of the PERK signaling pathway in the secondary brain injury (SBI) induced by intracerebral hemorrhage (ICH) and its potential mechanisms were investigated. Sprague-Dawley rats were used to establish ICH models by injecting autologous blood (100 µl). The PERK inhibitor GSK2606414 was injected intracerebroventricularly at 1 h after ICH and the eIF2α dephosphorylation inhibitor salubrinal, as an agonist of PERK downstream signaling pathway, was injected intraperitoneally at 30 min before ICH, respectively. It was revealed that with the treatment of GSK2606414 and salubrinal, the protein levels of p-eIF2α and ATF-4 were decreased and increased compared with ICH + vehicle (GSK2606414) and ICH + vehicle (salubrinal) group respectively (Figure 3A).

Reference: Front Neurosci. 2018 Feb 28;12:111. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5835756/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.