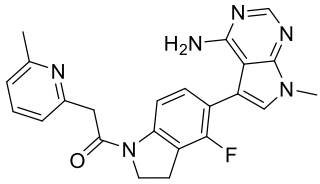
Product data sheet

MedKoo Cat#: 406230 Name: GSK2656157 CAS#: 1337532-29-2 Chemical Formula: $C_{23}H_{21}FN_6O$ Exact Mass: 416.17609 Molecular Weight: 416.45	
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:
GSK2656157 is an ATP-competitive inhibitor of PERK enzyme activity with an IC50 of 0.9 nM. It is highly selective for PERK with IC50 values >100 nM against a panel of 300 kinases. GSK2656157 inhibits PERK activity in cells with an IC50 in the range of 10-30 nM as shown by inhibition of stress-induced PERK autophosphorylation, eIF2α substrate phosphorylation, together with corresponding decreases in ATF4 and CHOP proteins in multiple cell lines. Oral administration of GSK2656157 to mice shows a dose- and time-dependent pharmacodynamic response in pancreas as measured by PERK auto-phosphorylation.

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	33.78	81.11
DMSO:PBS (pH 7.2) (1:3)	0.25	0.60
DMF	10.0	24.01
Ethanol	2.0	4.80
1M HCl	100.0	240.12

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.40 mL	12.01 mL	24.01 mL
5 mM	0.48 mL	2.40 mL	4.80 mL
10 mM	0.24 mL	1.20 mL	2.40 mL
50 mM	0.05 mL	0.24 mL	0.48 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. Moore PC, Qi JY, Thamsen M, Ghosh R, Peng J, Gliedt MJ, Meza-Acevedo R, Warren RE, Hiniker A, Kim GE, Maly DJ, Backes BJ, Papa FR, Oakes SA. Parallel Signaling through IRE1α and PERK Regulates Pancreatic Neuroendocrine Tumor Growth and Survival. Cancer Res. 2019 Dec 15;79(24):6190-6203. doi: 10.1158/0008-5472.CAN-19-1116. Epub 2019 Oct 31. PMID: 31672843; PMCID: PMC6911642.
2. Krishnamoorthy J, Rajesh K, Mirzajani F, Kesoglidou P, Papadakis AI, Koromilas AE. Evidence for eIF2α phosphorylation-independent effects of GSK2656157, a novel catalytic inhibitor of PERK with clinical implications. Cell Cycle. 2014;13(5):801-6. doi: 10.4161/cc.27726. Epub 2014 Jan 8. PMID: 24401334; PMCID: PMC3979916.

In vivo study

1. Sen T, Saha P, Gupta R, Foley LM, Jiang T, Abakumova OS, Hitchens TK, Sen N. Aberrant ER Stress Induced Neuronal-IFNβ Elicits White Matter Injury Due to Microglial Activation and T-Cell Infiltration after TBI. J Neurosci. 2020 Jan 8;40(2):424-446. doi: 10.1523/JNEUROSCI.0718-19.2019. Epub 2019 Nov 6. PMID: 31694961; PMCID: PMC6948950.
2. Loeuillard E, El Mourabit H, Lei L, Lemoinne S, Housset C, Cadoret A. Endoplasmic reticulum stress induces inverse regulations of major functions in portal myofibroblasts during liver fibrosis progression. Biochim Biophys Acta Mol Basis Dis. 2018 Dec;1864(12):3688-3696. doi: 10.1016/j.bbadis.2018.10.008. Epub 2018 Oct 4. PMID: 30292633.

7. Bioactivity

Biological target:

GSK2656157 is an ATP-competitive inhibitor of protein kinase R (PKR)-like endoplasmic reticulum kinase (PERK) with an IC50 of 0.9 nM.

In vitro activity

When GyrB.PERK-expressing cells were treated with increasing concentrations of GSK2656157 in the presence of coumermycin, PERK inhibitor decreased eIF2α phosphorylation in a concentration-dependent manner (Fig. 1C). When GyrB.PKR cells were used, treatment with GSK2656157 did not have a similar robust effect on the inhibition of eIF2α phosphorylation, as in GyrB.PERK-expressing cells (Fig. 1D). These data indicated that GSK2656157 is a potent and rather specific PERK inhibitor in cells ectopically expressing a conditionally active form of the eIF2α kinase.

Reference: Cell Cycle. 2014 Mar 1; 13(5): 801–806. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3979916/

In vivo activity

STING phosphorylation in NeuN-positive cells was increased in the pericontusional cortex neurons of TBI mice compared with sham (Fig. 1B and Fig. 1-1C, D); however, phospho-STING expression was dramatically decreased after treatment with GSK2656157 following TBI (Fig. 1B and Fig. 1-1C,D). Similar to phospho-STING, phospho-TBK1 and phospho-IRF3 were also increased after TBI in the CX compared with sham (Fig. 1C,D, and Fig. 1-1E–H). TBI-mediated increase in phospho-TBK1 and phospho-IRF3 was considerably decreased by 3 d of GSK2656157 treatment following TBI (Fig. 1C,D, and Fig. 1-1E–H).

Reference: J Neurosci. 2020 Jan 8; 40(2): 424–446. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6948950/#B79

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.