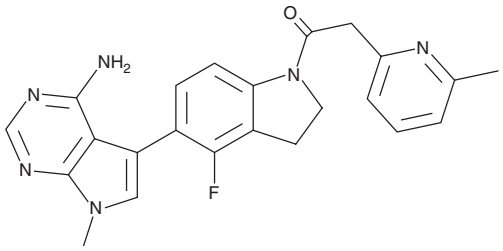
PRODUCT INFORMATION

GSK2656157

Item No. 17372

CAS Registry No.:	1337532-29-2
Formal Name:	1-[5-(4-amino-7-methyl-7H-pyrrolo[2,3-d] pyrimidin-5-yl)-4-fluoro-2,3-dihydro-1H-indol-1-yl]-2-(6-methyl-2-pyridinyl)-ethanone
MF:	$C_{23}H_{21}FN_6O$
FW:	416.5
Purity:	≥98%
UV/Vis.:	λ_{max}: 287 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

GSK2656157 is supplied as a crystalline solid. A stock solution may be made by dissolving the GSK2656157 in the solvent of choice, which should be purged with an inert gas. GSK2656157 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of GSK2656157 in ethanol is approximately 2 mg/ml and 10 mg/ml in DMSO and DMF.

GSK2656157 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, GSK2656157 should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. GSK2656157 has a solubility of approximately 0.25 mg/ml in a 1:3 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

GSK2656157 is an inhibitor of protein kinase R (PKR)-like endoplasmic reticulum kinase (PERK; IC_{50} = 0.9 nM).[1,2] It is selective for PERK over a panel of additional kinases.[1] GSK2656157 blocks both stress-induced PERK autophosphorylation and eIF2α substrate phosphorylation and decreases levels of ATF4 and CHOP in multiple cell lines.[1] It is orally bioavailable, suppressing PERK autophosphorylation in mouse pancreas and inhibiting the growth of multiple human tumor xenografts in mice.[1,2] GSK 2656157 inhibits caspase 1 activation in macrophage-like J774.1 cells, preventing LPS-induced IL-1β production, through its effects on the PERK/eIF2α pathway.[3]

References

1. Atkins, C., Minthorn, E., Zhang, S-Y., *et al.* Characterization of a Novel PERK Kinase Inhibitor with Antitumor and Antiangiogenic Activity. *Cancer Res.* **73(6)**, 1993-2002 (2012).
2. Axten, J., Romeril, S., Shu, A., *et al.* Discovery of GSK2656157: An Optimized PERK Inhibitor Selected for Preclinical Development. *ASC Med. Chem. Lett.* **4**, 964-968, (2013).
3. Ando, T., Komatsu, T., Naiki, Y., *et al.* GSK2656157, a PERK inhibitor, reduced LPS-induced IL-1β production through inhibiting Caspase 1 activation in macrophagelike J774.1 cells. *Immunopharmacol. Immunotoxicol.* **38(4)**, 298-302 (2016).

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