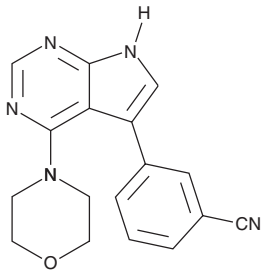
PRODUCT INFORMATION

PF-06447475

Item No. 18375

CAS Registry No.:	1527473-33-1
Formal Name:	3-[4-(4-morpholinyl)-7H-pyrrolo[2,3-d] pyrimidin-5-yl]-benzonitrile
MF:	$C_{17}H_{15}N_5O$
FW:	305.3
Purity:	≥98%
UV/Vis.:	λ_{max}: 224, 294 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

PF-06447475 is supplied as a crystalline solid. A stock solution may be made by dissolving the PF-06447475 in the solvent of choice, which should be purged with an inert gas. PF-06447475 is soluble in organic solvents such as DMSO and dimethyl formamide. The solubility of PF-06447475 in these solvents is approximately 2 and 5 mg/ml, respectively.

PF-06447475 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, PF-06447475 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. PF-06447475 has a solubility of approximately 0.12 mg/ml in a 1:7 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

PF-06447475 is an inhibitor of leucine-rich repeat kinase 2 (LRRK2; IC_{50} = 3 nM).[1] It also inhibits LRRK2 containing a glycine-to-serine substitution at position 2019 ($LRRK2^{G2019S}$; IC_{50} = 11 nM). PF-06447475 inhibits LRRK2 autoactivation in cells (IC_{50} = 25 nM). It inhibits paraquat-induced locomotor deficits, decreases in survival, and increases in cranial homogenate levels of malondialdehyde (MDA) in *D. melanogaster*.[2] PF-06447475 (30 mg/kg twice per day) increases the number of total and tyrosine hydroxylase-expressing neurons and decreases the number of inducible nitric oxide synthase-expressing neurons in rat substantia nigra pars compacta (SNPC) in a transgenic model of $Lrrk2^{G2019S}$- and α-synuclein-induced model of Parkinson's disease.[3] It reduces levels of macrophage infiltration in the ipsilateral SNPC in the same model at the same dose.

References

1. Henderson, J.L., Kormos, B.L., Hayward, M.M., *et al.* Discovery and preclinical profiling of 3-[4-(morpholin-4-yl)-7H-pyrrolo[2,3-d]pyrimidin-5-yl]benzonitrile (PF-06447475), a highly potent, selective, brain penetrant, and in vivo active LRRK2 kinase inhibitor. *J. Med. Chem.* **58(1)**, 419-432 (2015).
2. Quintero-Espinosa, D.A., Jimenez-Del-Rio, M., and Velez-Pardo, C. LRRK2 kinase inhibitor PF-06447475 protects Drosophila melanogaster against paraquat-induced locomotor impairment, life span reduction, and oxidative stress. *Neurochem. Res.* **49(9)**, 2440-2452 (2024).
3. Daher, J.P.L., Abdelmotilib, H.A., Hu, X., *et al.* Leucine-rich Repeat Kinase 2 (LRRK2) Pharmacological Inhibition Abates α-Synuclein Gene-induced Neurodegeneration. *J. Bio. Chem.* **290(32)**, 19433-19444 (2015).

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