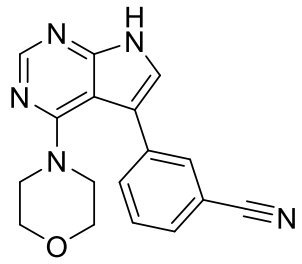
Product data sheet

MedKoo Cat#: 406655 Name: PF06447475 CAS#: 1527473-33-1 Chemical Formula: $C_{17}H_{15}N_5O$ Exact Mass: 305.12766 Molecular Weight: 305.33	
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:

PF06447475 is a highly potent, selective, brain penetrant, and in vivo active LRRK2 kinase inhibitor. Leucine rich repeat kinase 2 (LRRK2) has been genetically linked to Parkinson's disease (PD) by genome-wide association studies (GWAS). The most common LRRK2 mutation, G2019S, which is relatively rare in the total population, gives rise to increased kinase activity. As such, LRRK2 kinase inhibitors are potentially useful in the treatment of PD.

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	30.0	98.3

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.28 mL	16.38 mL	32.75 mL
5 mM	0.66 mL	3.28 mL	6.55 mL
10 mM	0.33 mL	1.64 mL	3.28 mL
50 mM	0.07 mL	0.33 mL	0.66 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. Mendivil-Perez M, Velez-Pardo C, Jimenez-Del-Rio M. Neuroprotective Effect of the LRRK2 Kinase Inhibitor PF-06447475 in Human Nerve-Like Differentiated Cells Exposed to Oxidative Stress Stimuli: Implications for Parkinson's Disease. Neurochem Res. 2016 Oct;41(10):2675-2692. doi: 10.1007/s11064-016-1982-1. Epub 2016 Jul 9. PMID: 27394417.
2. Henry AG, Aghamohammadzadeh S, Samaroo H, Chen Y, Mou K, Needle E, Hirst WD. Pathogenic LRRK2 mutations, through increased kinase activity, produce enlarged lysosomes with reduced degradative capacity and increase ATP13A2 expression. Hum Mol Genet. 2015 Nov 1;24(21):6013-28. doi: 10.1093/hmg/ddv314. Epub 2015 Aug 6. PMID: 26251043.

In vivo study

1. Rui Q, Ni H, Gao F, Dang B, Li D, Gao R, Chen G. LRRK2 Contributes to Secondary Brain Injury Through a p38/Drosha Signaling Pathway After Traumatic Brain Injury in Rats. Front Cell Neurosci. 2018 Mar 1;12:51. doi: 10.3389/fncel.2018.00051. PMID: 29545743; PMCID: PMC5837969.
2. Daher JP, Abdelmotilib HA, Hu X, Volpicelli-Daley LA, Moehle MS, Fraser KB, Needle E, Chen Y, Steyn SJ, Galatsis P, Hirst WD, West AB. Leucine-rich Repeat Kinase 2 (LRRK2) Pharmacological Inhibition Abates α-Synuclein Gene-induced Neurodegeneration. J Biol Chem. 2015 Aug 7;290(32):19433-44. doi: 10.1074/jbc.M115.660001. Epub 2015 Jun 15. PMID: 26078453; PMCID: PMC4528108.

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7. Bioactivity

Biological target:

PF-06447475 is a brain penetrant LRRK2 inhibitor with an IC_{50} of 3 nM.

In vitro activity

This study evaluated the effect of PF-475 (PF-06447475) on NCL exposed to ROT. As shown in Fig. 5, ROT significantly increased p-(S935)-LRRK2 levels compared to untreated NLCs (Fig. 5 a, b). In contrast, cells incubated with PF-475 alone (0.5, 1, 3 µM) or in the presence of ROT significantly reduced (S935)-LRRK2 kinase phosphorylation to control values (Fig. 5a–b). The total LRRK2 was affected neither by ROT nor by inhibitor alone (Fig. 5c). Similar results were obtained by IF analysis (Fig. 5d–g).

Reference: Neurochem Res. 2016 Oct;41(10):2675-2692. https://pubmed.ncbi.nlm.nih.gov/27394417/

In vivo activity

To determine whether LRRK2 played a role in regulating the p38 MAPK pathway and its downstream molecule Drosha, western blot analyses of the peri-injury cortex were performed, and changes in the protein levels of p-p38 and Drosha were quantified following LRRK2 inhibition or overexpression at 12 h after TBI or sham surgery. Results demonstrated that LRRK2 inhibitor PF-475 (PF06447475) decreased p-p38 expression in a dose-dependent manner ($F(5,30) = 27.13$, $P < 0.05$, Figures 6A,C), whereas LRRK2 overexpression significantly enhanced the p-p38 level. Conversely, the expression of Drosha, which was upregulated with the PF-475 treatment ($F(5,30) = 21.58$, $P < 0.05$, Figures 6B,D) and greatly downregulated in the LRRK2 overexpression group ($P < 0.05$), showed an opposite trend to that of p-p38.

Reference: Front Cell Neurosci. 2018; 12: 51. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5837969/

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.