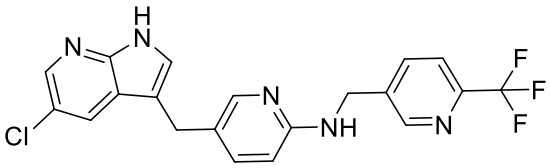
Product data sheet

MedKoo Cat#: 206178 Name: Pexidartinib (PLX3397) CAS#: 1029044-16-3 (free base) Chemical Formula: $C_{20}H_{15}ClF_3N_5$ Exact Mass: 417.09681 Molecular Weight: 417.81	
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:
Pexidartinib, also know as PLX-3397, is a CSF1R inhibitor with IC50 of 20 nM in development by Plexxikon for the treatment of tenosynovial giant cell tumors. It is in a phase 3 clinical trial for Pigmented Villonodular Synovitis (PVNS) or Giant Cell Tumor of the Tendon Sheath (GCT-TS).

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	20.0	47.87
DMF:PBS (pH 7.2) (1:3)	0.25	0.60
DMSO	42.67	102.13

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.39 mL	11.97 mL	23.93 mL
5 mM	0.48 mL	2.39 mL	4.79 mL
10 mM	0.24 mL	1.20 mL	2.39 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. Murga-Zamalloa C, Rolland DCM, Polk A, Wolfe A, Dewar H, Chowdhury P, Onder O, Dewar R, Brown NA, Bailey NG, Inamdar K, Lim MS, Elenitoba-Johnson KSJ, Wilcox RA. Colony-Stimulating Factor 1 Receptor (CSF1R) Activates AKT/mTOR Signaling and Promotes T-Cell Lymphoma Viability. Clin Cancer Res. 2020 Feb 1;26(3):690-703. doi: 10.1158/1078-0432.CCR-19-1486. Epub 2019 Oct 21. PMID: 31636099; PMCID: PMC7002219.
2. Liu Y, Given KS, Dickson EL, Owens GP, Macklin WB, Bennett JL. Concentration-dependent effects of CSF1R inhibitors on oligodendrocyte progenitor cells ex vivo and in vivo. Exp Neurol. 2019 Aug;318:32-41. doi: 10.1016/j.expneurol.2019.04.011. Epub 2019 Apr 25. PMID: 31029597; PMCID: PMC6615458.

In vivo study

1. Boyd MM, Litscher SJ, Seitz LL, Messing A, Hagemann TL, Collier LS. Pexidartinib treatment in Alexander disease model mice reduces macrophage numbers and increases glial fibrillary acidic protein levels, yet has minimal impact on other disease phenotypes. J Neuroinflammation. 2021 Mar 8;18(1):67. doi: 10.1186/s12974-021-02118-x. PMID: 33685480; PMCID: PMC7941726.

7. Bioactivity

Product data sheet

Biological target:

ATP-competitive CSF1R and c-Kit inhibitor, with IC50s of 20 and 10 nM

In vitro activity

Having established the expression and activation of CSF1R in TCL, a loss-of-function strategy was adopted to address its potential oncogenic role in these TCL using complementary molecular and pharmacologic approaches. The first compound used was a clinically available and rationally designed tyrosine kinase inhibitor that is selective for CSF1R (Pexidartinib, PLX3397). In order to confirm CSF1R inhibition upon pexidartinib treatment, TCL cells with autocrine-activation of CSF1R were treated with pexidartinib. A marked decrease in CSF1R phosphorylation was observed upon treatment with pexidartinib (Figure 2A, supplementary figure 4A). Importantly, pexidartinib did not show any effect on the phosphorylation levels of the oncogenic kinase NPM-ALK which is expressed in a portion of the TCL cells evaluated (supplementary figure 4B). In addition, a dose-dependent decrease in proliferation was observed with exposure to pexidartinib (Figure 2B and supplementary figure 4D–E), however these effects were not observed in TCL cells that do not express CSF1R, supporting the relative selectivity of this FDA-approved agent (supplementary figure 4C). Consistent with these findings, treatment with pexidartinib was associated with increased apoptosis of TCL cells, as demonstrated by phosphatidylserine exposure (Figure 2C–E), PARP cleavage and Caspase 3 cleavage (Figure 2F and supplementary figure 4F).

Reference: Clin Cancer Res. 2020 Feb 1; 26(3): 690–703. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7002219/

In vivo activity

To determine if treatment with the CSF1R inhibitor pexidartinib (PEX) depletes macrophages, PEX was administered via chow fed to GfapR236H/+ AxD model mice for a period of 2.5 months, beginning at weaning. Previous reports indicate that PEX treatment can raise GFAP levels in wild-type mice; therefore, wild-type (WT, Gfap+/+) littermates were also fed PEX or control chow as a comparison. The numbers of macrophages (IBA1+ cells) were counted in the olfactory bulb glomerular layer and the dentate gyrus of the hippocampus, areas that have been observed to display Rosenthal fibers in histological analyses. As expected, significant increases in the number of IBA1+ cells were observed in both regions in AxD compared to WT animals fed control chow (Fig.2a and b, representative images: Additional figure 1a and b). PEX treatment of AxD mice resulted in depletion of macrophages in both brain regions (Fig.2a and b). PEX treatment in WT mice did reduce macrophage numbers in the dentate gyrus, but not in a statistically significant manner in the olfactory bulb glomerular layer (Fig.2a and b). RT-qPCR for Aif1 (the gene encoding IBA1) revealed a similar decrease in PEX-treated mice (Fig.2c and d). Together, these data indicate that PEX treatment reduces brain macrophage numbers in AxD mice and may have region specific effects in WT mice.

Reference: J Neuroinflammation. 2021; 18: 67. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7941726/

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.