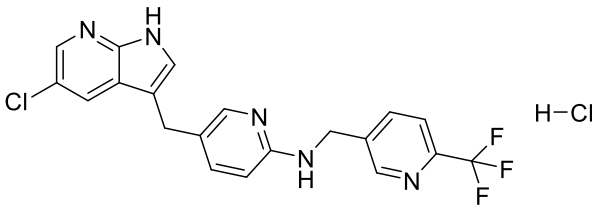
Product data sheet

MedKoo Cat#: 207104 Name: Pexidartinib HCl CAS#: 2040295-03-0 (HCl) Chemical Formula: $C_{20}H_{16}Cl_2F_3N_5$ Molecular Weight: 454.28	
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
DMSO	60.0	132.1

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.20 mL	11.01 mL	22.01 mL
5 mM	0.44 mL	2.20 mL	4.40 mL
10 mM	0.22 mL	1.10 mL	2.20 mL
50 mM	0.04 mL	0.22 mL	0.44 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.Park S, Kim M, Zhu J, Lee WK, Altan-Bonnet G, Meltzer P, Cheng SY. Inflammation suppression prevents tumor cell proliferation in a mouse model of thyroid cancer. Am J Cancer Res. 2020 Jun 1;10(6):1857-1870. PMID: 32642296; PMCID: PMC7339265.
2. Kurelac I, Iommarini L, Vatrinet R, Amato LB, De Luise M, Leone G, Girolimetti G, Umesh Ganesh N, Bridgeman VL, Ombrato L, Columbaro M, Ragazzi M, Gibellini L, Sollazzo M, Feichtinger RG, Vidali S, Baldassarre M, Foriel S, Vidone M, Cossarizza A, Grifoni D, Kofler B, Malanchi I, Porcelli AM, Gasparre G. Inducing cancer indolence by targeting mitochondrial Complex I is potentiated by blocking macrophage-mediated adaptive responses. Nat Commun. 2019 Feb 22;10(1):903. doi: 10.1038/s41467-019-08839-1. PMID: 30796225; PMCID: PMC6385215.

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7. Bioactivity

Biological target:

Pexidartinib hydrochloride (PLX-3397 hydrochloride) is a factor 1 receptor (CSF1R or M-CSFR) and c-Kit inhibitor with IC50 values of 10 nM (c-Kit) and 20 nM (cFMS).

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

This study tested whether attenuating the inflammatory responses could mitigate thyroid cancer progression. The mice were treated with an inhibitor of colony-stimulating factor 1 receptor (CSF1R), pexidartinib (PLX-3397; PLX). CSF1R mediates the activity of the cytokine, colony stimulating factor 1 (CSF1), in the production, differentiation, and functions of monocytes and macrophages. Treatment of PLX3397 (Pexidartinib; BOC Sciences Shirley, NY) was started from 6- to 7-weeks old. Mice were given PLX3397 doses of 50 mg/kg via oral gavage daily for 10 days. PLX3397 was dissolved in 10% DMSO and corn oil (sigma-Aldrich, St. Louis, MO). Treatment with PLX decreased 94% and 62% of inflammatory monocytes in the thyroid and bone marrow, respectively, versus controls. Further, PLX suppressed the expression of critical cytokine and inflammation-regulating genes such as Csf1r, SPP1 (OPN), Aif1, IL6, Ccl9, Ccl3, Ccl12, and Ccr2 (25%-80%), resulting in inhibition of 89% tumor cell proliferation, evidenced by Ki-67 immunostaining. These preclinical findings suggest that inflammation occurs in the early stage of thyroid carcinogenesis and plays a critical in cancer progression. Importantly, attenuation of inflammation by inhibitors such as PLX would be beneficial in preventing thyroid cancer.

Reference: Am J Cancer Res. 2020; 10(6): 1857–1870.https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7339265/

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.