Pexidartinib

Cat. No.: HY-16749

CAS No.: 1029044-16-3

Molecular Formula: $C_{20}H_{15}ClF_3N_5$

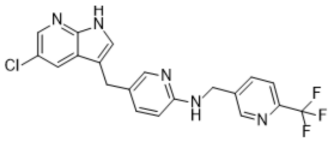
Molecular Weight: 417.81

Target: c-Fms; c-Kit; Apoptosis

Pathway: Protein Tyrosine Kinase/RTK; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	1 year
	-20°C	6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (239.34 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3934 mL	11.9672 mL	23.9343 mL
	5 mM	0.4787 mL	2.3934 mL	4.7869 mL
	10 mM	0.2393 mL	1.1967 mL	2.3934 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: 5 mg/mL (11.97 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.98 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.98 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.98 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Pexidartinib (PLX-3397) is a potent, orally active, selective, and ATP-competitive colony stimulating factor 1 receptor (CSF1R or M-CSFR) and c-Kit inhibitor, with IC_{50}s of 20 and 10 nM, respectively. Pexidartinib (PLX-3397) exhibits 10- to 100-fold selectivity for c-Kit and CSF1R over other related kinases. Pexidartinib (PLX-3397) induces cell apoptosis and has anti-tumor activity[1].

IC_{50} & Target	IC50: 10 nM (c-Kit), 20 nM (cFMS), 160 nM (FLT3), 350 nM (KDR), 860 nM (LCK), 880 nM (FLT1), 890 nM (NTRK3)[1]
In Vitro	Pexidartinib (PLX-3397) is a potent, selective and ATP-competitive CSF1R (cFMS) and c-Kit inhibitor, shows 10- to 100-fold selectivity for c-Kit and CSF1R over other related kinases, such as FLT3, KDR (VEGFR2), LCK, FLT1 (VEGFR1) and NTRK3 (TRKC), with IC_{50}s of 160, 350, 860, 880, and 890 nM, respectively[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Pexidartinib can be used to deplete the microglia cells in mice. Pexidartinib (290 ppm in AIN-76A standard chow, 21 days) depletes the microglia cells in brain by 70% in adult male C57BL/6 J mice (20–25 g)[5]. Pexidartinib (600 ppm in chow, 10 days and 30 days) depletes the microglia cells more than 90% in brain of C57BL/6J mice [6]. Pexidartinib (PLX3397; 0.25, 1 mg/kg, twice daily for 8 days) inhibits the proliferation of microglia and BrdU-positive cells in neonatal mice[2]. Pexidartinib (1 mg/kg, twice daily for 8 day) shows no obvious effect on the cleaved caspase-3-positive cells in mice[2]. Pexidartinib (50 mg/kg; p.o.; every second day for 3 weeks) reduces tissue macrophage levels without affecting glucose homeostasis in mice[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Neonatal mice[2]
Dosage:	0.25, 1 mg/kg
Administration:	I.P. twice daily for 8 days
Result:	Decreased the number of microglia and BrdU-positive proliferative cells, but did not change the cleaved caspase-3-positive cells.

Animal Model:	10-week old litter mate C57BL/6 mice (chow and high-fat diet fed mice)[4]
Dosage:	50 mg/kg
Administration:	P.o.; every second day for 3 weeks
Result:	Substantially reduced macrophage numbers in adipose tissue of both chow and high-fat diet fed mice without affecting total myeloid cell levels.

CUSTOMER VALIDATION

- Nature. 2024 Apr;628(8006):145-153.
- Nature. 2022 Mar;603(7899):138-144.
- Cancer Cell. 2023 Nov 13;41(11):1911-1926.e8.
- Cancer Cell. 2021 Sep 1;S1535-6108(21)00445-1.
- Nat Immunol. 2023 May;24(5):827-840.

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REFERENCES

[1]. Luo L, et al. Intermittent theta-burst stimulation improves motor function by inhibiting neuronal pyroptosis and regulating microglial polarization via TLR4/NFκB/NLRP3 signaling pathway in cerebral ischemic mice. J Neuroinflammation. 2022 Jun 11;19(1):141.

[2]. Chadarevian JP, et al. Engineering an inhibitor-resistant human CSF1R variant for microglia replacement. J Exp Med. 2023 Mar 6;220(3):e20220857.

[3]. DeNardo DG, et al. Leukocyte complexity predicts breast cancer survival and functionally regulates response to chemotherapy. Cancer Discov. 2011 Jun;1(1):54-67.

[4]. Kuse Y, et al. Microglia increases the proliferation of retinal precursor cells during postnatal development. Mol Vis. 2018 Jul 30;24:536-545. eCollection 2018.

[5]. Lee JH, et al. A phase I study of pexidartinib, a colony-stimulating factor 1 receptor inhibitor, in Asian patients with advanced solid tumors. Invest New Drugs. 2019 Mar 2.

[6]. Merry TL, et al. The CSF1 receptor inhibitor pexidartinib (PLX3397) reduces tissue macrophage levels without affecting glucose homeostasis in mice. Int J Obes (Lond). 2020;44(1):245-253.

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