PF-04217903 mesylate

Cat. No.: HY-12017A

CAS No.: 956906-93-7

Molecular Formula: $C_{20}H_{20}N_8O_4S$

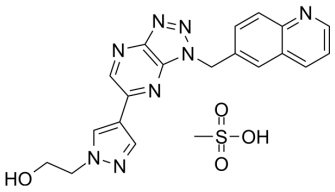
Molecular Weight: 468.49

Target: c-Met/HGFR

Pathway: Protein Tyrosine Kinase/RTK

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (106.73 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1345 mL	10.6726 mL	21.3452 mL
	5 mM	0.4269 mL	2.1345 mL	4.2690 mL
	10 mM	0.2135 mL	1.0673 mL	2.1345 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 3 mg/mL (6.40 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 3 mg/mL (6.40 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PF-04217903 mesylate is a potent ATP-competitive c-Met kinase inhibitor with K_i of 4.8 nM for human c-Met. PF-04217903 mesylate shows more than 1,000-fold selectivity relative to 208 kinases. Antiangiogenic properties[1][2].

IC_{50} & Target

Ki: 4.8 nM (human c-Met)[1]

In Vitro

PF-04217903 mesylate (0.1-10000 nM; 48-72 hours) inhibits proliferation of c-Met–amplified human GTL-16 gastric carcinoma and H1993 NSCLC cells with IC_{50} values of 12 and 30 nM, respectively[1].
PF-04217903 mesylate induces apoptosis of GTL-16 cells (IC_{50}=31 nM) [1].
PF-04217903 mesylate also inhibits HGF-mediated cell migration and Matrigel invasion in several c-Met–overexpressing tumor cell lines such as human NCI-H441 lung carcinoma and HT29 colon carcinoma with IC50 values comparable with those for inhibition of c-Met phosphorylation in these cell lines (IC_{50}= 7-12.5 nM)[1].

PF-04217903 mesylate displays similar potency to inhibit the activity of c-Met-H1094R, c-Met-R988C, and c-Met-T1010I with IC_{50} of 3.1 nM, 6.4 nM, and 6.7 nM, respectively, but has no inhibitory activity against c-Met-Y1230C with IC_{50} of >10 μM[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	GTL-16, H1993 cells
Concentration:	0.1, 1, 10, 100, 1000, 10000 nM
Incubation Time:	48-72 hours
Result:	Inhibited proliferation of c-Met–amplified human GTL-16 gastric carcinoma and H1993 NSCLC cells with IC_{50} values of 12 and 30 nM, respectively.

Apoptosis Analysis[1]

Cell Line:	GTL-16 cells
Concentration:	1.5-3333 nM
Incubation Time:	48 hours
Result:	Induced apoptosis of GTL-16 cells (IC_{50}=31 nM).

In Vivo

PF-04217903 mesylate (1-30 mg/kg; p.o.; daily for 16 days) shows dose-dependent tumor growth inhibition, which correlated with the inhibition in c-Met phosphorylation in these tumors [1].

PF-04217903 mesylate (5-50 mg/kg, p.o.; once daily for 3 days) dose dependently inhibits c-Met, Gab-1, Erk1/2, and AKT phosphorylation and induced apoptosis (cleaved caspase-3) in U87MG xenograft tumors at all dose levels. PF-04217903 mesylate shows a significant dose-dependent reduction of human IL-8 levels in both the U87MG and GTL-16 models and decreases human VEGFA levels in the GTL-16 model. PF-04217903 mesylate strongly induces phospho-PDGFRβ levels in U87MG xenograft tumors[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female nu/nu mice GTL-16 xenograft model[1]
Dosage:	1, 3, 10, 30 mg/kg
Administration:	Oral; daily for 16 days
Result:	Showed dose-dependent tumor growth inhibition, and was correlated with the inhibition in c-Met phosphorylation in these tumors.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Harvard Medical School LINCS LIBRARY

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REFERENCES

[1]. Timofeevski SL, et al. Enzymatic characterization of c-Met receptor tyrosine kinase oncogenic mutants and kinetic studies with aminopyridine and triazolopyrazine

inhibitors. Biochemistry, 2009, 48(23), 5339-5349.

[2]. Shojaei F, et al. HGF/c-Met acts as an alternative angiogenic pathway in sunitinib-resistant tumors. Cancer Res, 2010, 70(24), 10090-10100.

[3]. Krumbach R, et al. Primary resistance to cetuximab in a panel of patient-derived tumour xenograft models: activation of MET as one mechanism for drug resistance. Eur J Cancer, 2011, 47(8), 1231-1243.

Caution: Product has not been fully validated for medical applications. For research use only.

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