Gedatolisib

Cat. No.: HY-10681

CAS No.: 1197160-78-3

Molecular Formula: $C_{32}H_{41}N_9O_4$

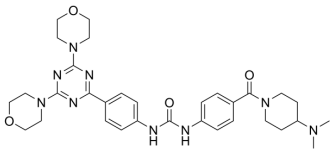
Molecular Weight: 615.73

Target: PI3K; mTOR

Pathway: PI3K/Akt/mTOR

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 4 mg/mL (6.50 mM; Need warming)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.6241 mL	8.1204 mL	16.2409 mL
5 mM	0.3248 mL	1.6241 mL	3.2482 mL
10 mM	---	---	---

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

BIOLOGICAL ACTIVITY

Description

Gedatolisib (PKI-587) is a highly potent dual inhibitor of PI3Kα, PI3Kγ, and mTOR with IC_{50}s of 0.4 nM, 5.4 nM and 1.6 nM, respectively[1]. Gedatolisib is equally effective in both complexes of mTOR, mTORC1 and mTORC2[2].

IC_{50} & Target

PI3Kα 0.4 nM (IC_{50})	PI3Kα-H1047R 0.6 nM (IC_{50})	PI3Kα-E545K 0.6 nM (IC_{50})	PI3Kγ 5.4 nM (IC_{50})
PI3Kβ 6 nM (IC_{50})	PI3Kδ 6 nM (IC_{50})	mTOR 1.6 nM (IC_{50})	mTORC1
mTORC2			

In Vitro

Gedatolisib (PKI-587) shows good potency in cell growth inhibition assays using MDA-361 and PC3-MM2 cell lines with IC_{50}s of 4.0 and 13.1 nM, respectively[1].

Gedatolisib shows potent suppression of phosphorylation of PI3K/mTOR signaling pathway proteins in MDA-361 tumor cells.

Gedatolisib (0.03-3 μM; 4 hours) prevents the phosphorylation of Akt at Thr 308 and induces cleaved PARP at 30 nM[1].

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

Western Blot Analysis[1]

Cell Line:	MDA-361 tumor cells
Concentration:	0.03, 0.1, 0.3, 1, and 3 μM
Incubation Time:	4 hours
Result:	Prevented the phosphorylation of Akt (pAkt) at threonine 308 (T308; IC_{50}=8 nM).

In Vivo

Gedatolisib (PKI-587; administered i.v. at 20 mg/kg on days 1, 5, 9) exhibits potent antitumor efficacy against MDA-361 tumors in mice[1].

Gedatolisib exhibits terminal elimination half-life ($T_{1/2}$ 14.4 h) due to high plasma clearance (7 mL/min/kg) combined with large volumes of distribution (7.2 L/kg respectively) following i.v. administration (25 mg/kg) female nude mice[1].

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

Animal Model:	Female nude mice bearing MDA-361 xenograft model[1].
Dosage:	20 mg/kg
Administration:	Administered i.v. at 20 mg/kg on an intermittent regimen (days 1, 5, 9).
Result:	Caused regression of large staged (~900 mm^3) tumors. The minimum efficacious dose (MED) was determined to be 3 mg/kg against MDA-361 tumors and maximum tolerated single dose (MTD) was determined to be 30 mg/kg.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Nat Commun. 2021 Aug 25;12(1):5112.
- Am J Transl Res. 2019 Aug 15;11(8):5134-5149.
- Molecules. 2020 Apr 23;25(8):1980.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Venkatesan AM, et al. Bis(morpholino-1,3,5-triazine) derivatives: potent adenosine 5'-triphosphate competitive phosphatidylinositol-3-kinase/mammalian target of rapamycin inhibitors: discovery of compound 26 (PKI-587), a highly efficacious dual inhibitor. J Med Chem. 2010, 53(6), 2636-2645.

[2]. Freitag H, et al. Inhibition of mTOR's Catalytic Site by PKI-587 Is a Promising Therapeutic Option for Gastroenteropancreatic Neuroendocrine Tumor Disease. Neuroendocrinology. 2017;105(1):90-104.

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

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA