GDC-0326

Cat. No.: HY-101272

CAS No.: 1282514-88-8

Molecular Formula: $C_{19}H_{22}N_6O_3$

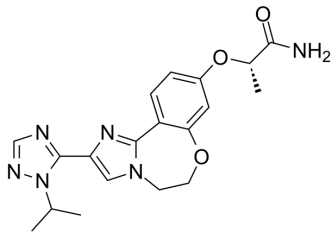
Molecular Weight: 382.42

Target: PI3K

Pathway: PI3K/Akt/mTOR

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (261.49 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.6149 mL	13.0746 mL	26.1493 mL
5 mM	0.5230 mL	2.6149 mL	5.2299 mL
10 mM	0.2615 mL	1.3075 mL	2.6149 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: ≥ 2.5 mg/mL (6.54 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.54 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.54 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GDC-0326 is a potent and selective PI3Kα inhibitor with a K_i of 0.2 nM.

IC_{50} & Target

PI3Kα	PI3Kδ	PI3Kγ	PI3Kβ
0.2 nM (Ki)	4 nM (Ki)	10.2 nM (Ki)	26.6 nM (Ki)

In Vitro

GDC-0326 is highly selective over other kinases. In a panel of 235 kinases, only one is inhibited by >50% by GDC-0326 when

	tested at 1 μM. GDC-0326 is not an inhibitor of cytochrome P450 enzymes tested (IC_{50}>10 μM against 3A4, 2C9 1A2, 2C19, 2D6), is highly permeable in MDCK cells and has thermodynamic solubility of 82 μg/mL at pH 7.4[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	GDC-0326 is highly stable in human and rat liver microsomes, and there is a good correlation with in vivo rat clearance. It is found to have consistently low clearance and high oral bioavailability across species tested, enabling significant sustained free drug levels. Daily administration of GDC-0326 orally at 0.78, 1.56, 3.25, 6.25, or 12.5 mg/kg results in dose-dependent increase in TGI (73%, 79%, 83%, 101%, and 110%, respectively) and tumor regressions (6 PRs out of 10 animal at 6.25 and 12.5 mg/kg) when compared to vehicle treated mice. Daily administration of GDC-0326 orally at 0.78, 1.56, 3.25, 6.25, or 12.5 mg/kg also results in dose-dependent increase in TGI (73%, 97%, 97%, 122%, and 121%, respectively) in the KPL-4 xenograft model. Notably, maximum efficacy of GDC-0326 is observed at 6.25 mg/kg in the KPL-4 model based on TGI and tumor regressions (9 PRs and 1 CR out of 10 animal treated) when compared to vehicle treated mice. Doses of GDC-0326 up to 12.5 mg/kg are well tolerated based on less than 10% body weight loss (data not shown)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Rats: Male Sprague-Dawley rats are dosed intravenously with 1 mg/kg of GDC-0326 prepared in 60% PEG400/10% Ethanol. Male Sprague-Dawley rats are dosed PO with 5 mg/kg of GDC-0326 in 0.5% methylcellulose with 0.2% Tween 80 (MCT)[1]. Mice: Female NCR nude mice are dosed intravenously with 1 mg/kg of GDC-0326 prepared in 60% PEG400/10% Ethanol and PO at 25 mg/kg in 0.5% methylcellulose with 0.2% Tween 80 (MCT)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Heffron TP, et al. The Rational Design of Selective Benzoxazepin Inhibitors of the α-Isoform of Phosphoinositide 3-Kinase Culminating in the Identification of (S)-2-((2-(1-Isopropyl-1H-1,2,4-triazol-5-yl)-5,6-dihydrobenzo[f]imidazo[1,2-d][1,4]oxazepin-9-y

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