Dactolisib Tosylate

Cat. No.: HY-15174

CAS No.: 1028385-32-1

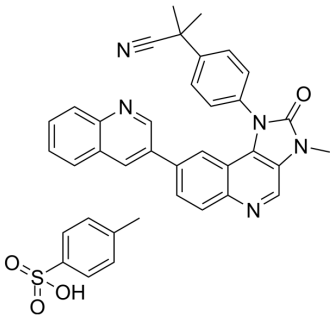
Molecular Formula: $C_{37}H_{31}N_5O_4S$

Molecular Weight: 641.74

Target: PI3K; mTOR; Autophagy

Pathway: PI3K/Akt/mTOR; Autophagy

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 1 years; -20°C, 6 months (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 34 mg/mL (52.98 mM; Need ultrasonic and warming)
H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.5583 mL	7.7913 mL	15.5826 mL
	5 mM	0.3117 mL	1.5583 mL	3.1165 mL
	10 mM	0.1558 mL	0.7791 mL	1.5583 mL

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

In Vivo

1. Add each solvent one by one: 50% PEG300 >> 50% saline
   Solubility: 16.67 mg/mL (25.98 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1 mg/mL (1.56 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Dactolisib Tosylate (BEZ235 Tosylate) is a dual PI3K and mTOR kinase inhibitor with IC_{50} values of 4, 75, 7, 5 nM for PI3Kα, β, γ, δ, respectively. Dactolisib Tosylate (BEZ235 Tosylate) inhibits mTORC1 and mTORC2.

IC_{50} & Target

p110α 4 nM (IC_{50})	p110α-H1047R 4.6 nM (IC_{50})	p110α-E545K 5.7 nM (IC_{50})	p110γ 5 nM (IC_{50})
p110δ 7 nM (IC_{50})	p110β 75 nM (IC_{50})	mTOR 20.7 nM (IC_{50})	mTORC1
mTORC2	Autophagy		

In Vitro	Dactolisib (BEZ235) is an imidazo[4,5-c]quinoline derivative that inhibits PI3K and mTOR kinase activity by binding to the ATP-binding cleft of these enzymes. The IC_{50}s for PI3Kα, β, γ, δ are 4, 75, 7, 5 nM, respectively. It is also found to be as active against the mutant $PI3K\alpha^{E545K}$ or $PI3K\alpha^{H1047R}$ with IC_{50}s of 5.7 and 4.6 nM, respectively. In human tumor cell lines, it is able to effectively and specifically block the dysfunctional activation of the PI3K pathway, inducing G1 arrest. PTEN-null cell lines PC3M and U87MG shows a dose-dependent reduction in cell proliferation when treated with increasing concentrations of Dactolisib (BEZ235), with an average GI_{50} of 10 to 12 nM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Dactolisib (BEZ235) is well tolerated, displays disease stasis when administered orally, and enhances the efficacy of other anticancer agents. At a dose of 50 mg/kg, Dactolisib (BEZ235) appears rapidly in plasma with a C_{max} of 1.68 μM at 0.5 h and a C_{24h} of 0.03 μM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Mice: The NVP-Dactolisib (BEZ235) powder is dissolved in NMP on sonication, and the remaining volume of polyethylene glycol 300 is added to a concentration of 5 mg/mL. The application volume is 10 mL/kg. For analytics, frozen tissues are minced and then homogenized in an equal volume of ice-cold PBS and centrifugation, supernatants are analyzed. Samples are then eluted with a linear gradient of 10% to 90% (v/v) acetonitrile in water containing 0.05% (v/v) trifluoroacetic acid over a period of 20 min at a flow rate of 1 mL/min. The compounds are detected by UV absorbance at 340 nm, and concentrations are determined by the external standard method using peak heights[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nature. 2018 Aug;560(7719):499-503.
- Cell Res. 2019 Nov;29(11):895-910.
- Blood. 2019 Oct 17;134(16):1323-1336.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Nat Commun. 2017 Jun 8;8:15617.

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REFERENCES

[1]. Maira SM, et al. Identification and characterization of NVP-BEZ235, a new orally available dual phosphatidylinositol 3-kinase/mammalian target of rapamycin inhibitor with potent in vivo antitumor activity. Mol Cancer Ther, 2008, 7(7), 1851-1863.

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