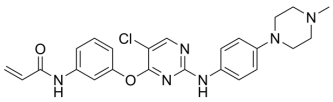
WZ-3146

Cat. No.:	HY-12001
CAS No.:	1214265-56-1
Molecular Formula:	$C_{24}H_{25}ClN_6O_2$
Molecular Weight:	464.95
Target:	EGFR
Pathway:	JAK/STAT Signaling; Protein Tyrosine Kinase/RTK
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 : 62.5 mg/mL (134.42 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1508 mL	10.7538 mL	21.5077 mL
	5 mM	0.4302 mL	2.1508 mL	4.3015 mL
	10 mM	0.2151 mL	1.0754 mL	2.1508 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 (5.38 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.38 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.38 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

WZ3146 is a mutant selective EGFR inhibitor with IC_{50}s of 2, 2, 5, 14 and 66 nM for $EGFR^{L858R}$, $EGFR^{L858R/T790M}$, $EGFR^{E746\_A750}$, $EGFR^{E746\_A750/T790M}$ and EGFR, respectively.

IC_{50} & Target

$EGFR^{L858R}$ 2 nM (IC_{50})	$EGFR^{L858R/T790M}$ 5 nM (IC_{50})	$EGFR^{E746\_A750}$ 2 nM (IC_{50})	$EGFR^{E746\_A750/T790M}$ 14 nM (IC_{50})
EGFR 24 nM (IC_{50})			

In Vitro	WZ3146 is a novel EGFR inhibitor, suppresses the growth of EGFR T790M containing cell lines and inhibits EGFR phosphorylation[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	In vitro inhibitory enzyme kinetic assays are carried out in triplicate using the ATP/NADH coupled assay system in a 96-well format. The final reaction mixture contains 0.5mg/mL Bovine Serum Albumin (BSA), 2mM $MnCl_2$, 1mM phospho(enol) pyruvic acid, 1mM TCEP, 0.1M Hepes 7.4, 2.5mM poly-[Glu4Tyr1] peptide, 1/50 of the final reaction mixture volume of pyruvate kinase/lactic dehydrogenase enzymes from rabbit muscle, 0.5mM NADH, 0.5μM EGFR kinase, 100μM ATP and varied amount of inhibitors. Inhibitors and ATP are mixed and made separate stock from the mixture with all other ingredients and added last to the latter to start the reaction. Steady state initial velocity data are drawn from the slopes of the A340 curves[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Growth and inhibition of growth is assessed by MTS assay. Ba/F3 cells are exposed to WZ3146 treatment for 72 hours. Growth and inhibition of growth is assessed by MTS assay[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Zhou W, et al. Novel mutant-selective EGFR kinase inhibitors against EGFR T790M.Nature. 2009 Dec 24;462(7276):1070-4.

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