HKI-357

Cat. No.: HY-103443

CAS No.: 848133-17-5

Molecular Formula: $C_{31}H_{29}ClFN_5O_3$

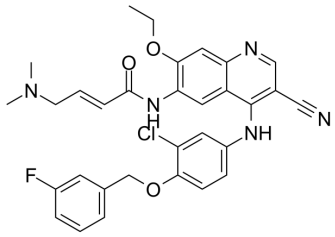
Molecular Weight: 574.05

Target: EGFR

Pathway: JAK/STAT Signaling; Protein Tyrosine Kinase/RTK

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (174.20 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7420 mL	8.7100 mL	17.4201 mL
	5 mM	0.3484 mL	1.7420 mL	3.4840 mL
	10 mM	0.1742 mL	0.8710 mL	1.7420 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 (4.36 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (4.36 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.36 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

HKI-357 is an irreversible dual inhibitor of EGFR and ERBB2 with IC_{50}s of 34 nM and 33 nM, respectively. HKI-357 suppresses EGFR autophosphorylation (at Y1068), and AKT and MAPK phosphorylation[1].

IC_{50} & Target

EGFR	ErbB2
34 nM (IC_{50})	33 nM (IC_{50})

In Vitro

HKI-357 (0.01-10 μM) is effective in suppressing ligand-induced EGFR autophosphorylation and its downstream signaling, as determined by AKT and MAPK phosphorylation in NCI-H1975 cells[1].

HKI-357 also is effective in suppressing EGFR autophosphorylation (measured at residue Y1068), and AKT and MAPK phosphorylation in parental NCI-H1650 cells harboring the delE746-A750 EGFR mutation[1].

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

Western Blot Analysis[1]

Cell Line:	NCI-H1975 bronchoalveolar cell line
Concentration:	0.01, 0.01, 0.1, 1 and 10 μM
Incubation Time:	
Result:	Suppressed ligand-induced EGFR autophosphorylation and its downstream signaling AKT and MAPK phosphorylation.

REFERENCES

[1]. Kwak EL, et al. Irreversible inhibitors of the EGF receptor may circumvent acquired resistance to gefitinib. Proc Natl Acad Sci U S A. 2005 May 24;102(21):7665-70.

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