Neratinib

Cat. No.: HY-32721

CAS No.: 698387-09-6

Molecular Formula: $C_{30}H_{29}ClN_6O_3$

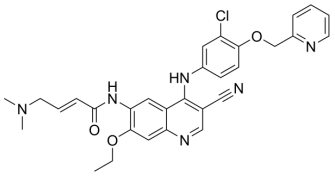
Molecular Weight: 557.04

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 : 13.33 mg/mL (23.93 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7952 mL	8.9760 mL	17.9520 mL
	5 mM	0.3590 mL	1.7952 mL	3.5904 mL
	10 mM	0.1795 mL	0.8976 mL	1.7952 mL

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

In Vivo

1. Add each solvent one by one: 0.5% MC >> 0.5% Tween-80
   Solubility: 3.33 mg/mL (5.98 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2 mg/mL (3.59 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 0.83 mg/mL (1.49 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Neratinib (HKI-272) is an orally available, irreversible, highly selective HER2 and EGFR inhibitor with IC_{50}s of 59 nM and 92 nM, respectively[1].

IC_{50} & Target

HER2	EGFR
59 nM (IC_{50})	92 nM (IC_{50})

In Vitro

Neratinib displays no activity against other serine-threonine kinases such as Akt, cyclin D1/cdk4, cyclin E/cdk2, cyclin

B1/cdk1, IKK-2, MK-2, PDK1, c-Raf, and Tpl-2, as well as the tyrosine kinase c-Met[1].
Neratinib (0.5 ng/mL–5 μg/mL, 2 days) inhibits the proliferation of cell lines that show high levels of HER-2 (3T3/neu, SK-Br-3, and BT474) and is much less active in cell lines that express neither HER-2 nor EGFR (3T3, MDA-MB-435, and SW620) [1].
Neratinib (0-2 nM, 12-16 h) arrests BT474 cell cycle at G1-S phase[1].
Neratinib results in the inhibition of MAPK and Akt phosphorylation, down-regulation of cyclin D1 levels, and induction of p27[1].

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

Cell Proliferation Assay[1]

Cell Line:	3T3, 3T3/neu, SK-Br-3, BT 474, A431, MDA-MB-435 and SW620
Concentration:	0.5 ng/mL–5 μg/mL
Incubation Time:	2 days (6 days for BT474)
Result:	Inhibited cell proliferation with IC_{50} values of 700 ± 78, 3 ± 0.14, 2 ± 0.18, 2 ± 0.06, 81± 9, 960 ± 165 and 690 ± 84 nM against 3T3, 3T3/neu, SK-Br-3, BT 474, A431, MDA-MB-435 and SW620 cells, respectively.

Western Blot Analysis[1]

Cell Line:	BT474 or A431 cells
Concentration:	0, 2, 10, 50, 100 and 200 nM
Incubation Time:	3 h
Result:	Decreased ligand-independent receptor phosphorylation by 50% (IC_{50}) at 5 nM in BT474 cells, repressed EGF-dependent phosphorylation of EGFR in A431 cells at a comparable dose (IC_{50} = 3 nM). Effectively repressed phosphorylation of MAPK and Akt in BT474 cells.

Cell Cycle Analysis[1]

Cell Line:	BT474
Concentration:	0–2 nM
Incubation Time:	12–16 h
Result:	Blocked cell cycle progression, causing a G1-S arrest, a 50% decrease in the number of cells in the S (DNA synthesis) phase of the cell cycle was observed at a concentration of 2 nM.

In Vivo

Neratinib (HKI-272) (0-80 mg/kg/day; i.g.; 42 days) shows anticancer activities against cancer cells that expresses high levels of HER-2 or EGFR[1].

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

Animal Model:	Female athymic (nude) mice, tumor xenograft[1]
Dosage:	10, 20, 40, 60 or 80 mg/kg/day
Administration:	Gavage, 42 days
Result:	Reduced tumor growth in a dose-dependent manner in 3T3/neu, BT474, SK-OV-3 and A431 xenografts, but was o inactive in xenografts of MX-1 and MCF-7. Inhibited phosphorylation

	of HER-2 in BT474 xenografts.

CUSTOMER VALIDATION

- Cancer Cell. 2024 Jan 8;42(1):101-118.e11.
- Ann Rheum Dis. 2020 Dec;79(12):1635-1643.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Sci Transl Med. 2018 Jun 20;10(446):eaao2565.
- Nat Commun. 2023 Nov 2;14(1):6997.

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REFERENCES

[1]. Rabindran SK, et al. Antitumor activity of HKI-272, an orally active, irreversible inhibitor of the HER-2 tyrosine kinase. Cancer Res, 2004, 64(11), 3958-3965.

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