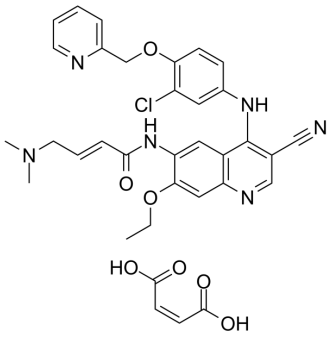
Neratinib maleate

Cat. No.:	HY-32721B
CAS No.:	915942-22-2
Molecular Formula:	$C_{34}H_{33}ClN_6O_7$
Molecular Weight:	673.11
Target:	EGFR
Pathway:	JAK/STAT Signaling; Protein Tyrosine Kinase/RTK
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (371.41 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.4856 mL	7.4282 mL	14.8564 mL
	5 mM	0.2971 mL	1.4856 mL	2.9713 mL
	10 mM	0.1486 mL	0.7428 mL	1.4856 mL

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

BIOLOGICAL ACTIVITY

Description

Neratinib (HKI-272) maleate 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

- 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.
- Cell Syst. 2019 Jul 24;9(1):35-48.e5.
- Cell Rep. 2022 Apr 5;39(1):110595.

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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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