DBPR112

Cat. No.: HY-128778

CAS No.: 1226549-49-0

Molecular Formula: $C_{32}H_{31}N_5O_3$

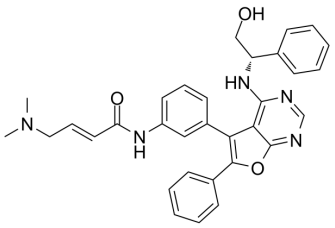
Molecular Weight: 533.62

Target: EGFR

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

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (468.50 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.8740 mL	9.3700 mL	18.7399 mL
5 mM	0.3748 mL	1.8740 mL	3.7480 mL
10 mM	0.1874 mL	0.9370 mL	1.8740 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: ≥ 2.08 mg/mL (3.90 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (3.90 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.90 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

DBPR112 is an orally active furanopyrimidine-based EGFR inhibitor with IC_{50}s of 15 nM and 48 nM for $EGFR^{WT}$ and $EGFR^{L858R/T790M}$, respectively. DBPR112 can occupy the ATP-binding site. DBPR112 has significant antitumor efficacy[1].

IC_{50} & Target

$EGFR^{WT}$	$EGFR^{L858R/T790M}$
15 nM (IC_{50})	48 nM (IC_{50})

In Vitro

DBPR112 (compound 78; 0.32-1000 nM; 16 hours) induces reduction of phosphorylated EGFR in a dose-dependent manner[1]

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DBPR112 shows the inhibitory activity against HCC827 (CC_{50}=25 nM), H1975 (CC_{50}=620 nM) and A431 Cell (CC_{50}=1.02 μM) cell lines[1].

DBPR112 occupies the ATP-binding site and interacts with surrounding residues by covalent bonding, hydrogen bonds, and hydrophobic interactions, which give it a potent inhibitory activity against WT EGFR[1].

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

Western Blot Analysis[1]

Cell Line:	H1975 cells
Concentration:	0.32, 1.6, 8.0, 40, 200, 1000 nM
Incubation Time:	16 hours
Result:	Induced reduction of phosphorylated EGFR in a dose-dependent manner in H1975 cells.

In Vivo

DBPR112 (orally; 20-50 mg/kg; 5 days/week for 2 consecutive weeks) significantly reduces tumor growth in HCC827 tumor model. DBPR112 (orally; 50 mg/kg; once a day for 15 days) has a significant antitumor effect (mean tumor growth inhibition of 34%) in H1975 tumor model[1].

DBPR112 (IV; 5 mg/kg) has a $T_{1/2}$ of 2.3 hours, a CL of 55.6 mL/min•kg, and a V_{ss} of 8.6 L/kg for rats[1].

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

Animal Model:	HCC827 tumor model (6- to 8-week-old athymic NU-Fox1nu nude mice)[1]
Dosage:	20, 50 mg/kg
Administration:	Orally; 5 days/week for 2 consecutive weeks (days 1-5 and 8-12)
Result:	Significantly reduced tumor growth.

Animal Model:	Rats[1]
Dosage:	5 mg/kg for IV and 20 mg/kg for PO (Pharmacokinetic Analysis)
Administration:	IV or PO
Result:	Had a $T_{1/2}$ of 2.3 hours, a CL of 55.6 mL/min•kg, and a V_{ss} of 8.6 L/kg by IV. Had a $T_{1/2}$ of 3.4 hours, a C_{max} of 508 ng/mL and an AUC of 2978 ng/mL•h by PO.

REFERENCES

[1]. Lin SY, et al. Discovery of a Furanopyrimidine-Based Epidermal Growth Factor Receptor Inhibitor (DBPR112) as a Clinical Candidate for the Treatment of Non-Small Cell Lung Cancer. J Med Chem. 2019 Nov 27;62(22):10108-10123.

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