Pelitinib

Cat. No.: HY-32718

CAS No.: 257933-82-7

Molecular Formula: $C_{24}H_{23}ClFN_5O_2$

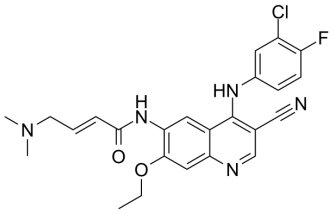
Molecular Weight: 467.92

Target: EGFR; Src

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 : 25 mg/mL (53.43 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1371 mL	10.6856 mL	21.3712 mL
	5 mM	0.4274 mL	2.1371 mL	4.2742 mL
	10 mM	0.2137 mL	1.0686 mL	2.1371 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 (5.34 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (5.34 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Pelitinib (EKB-569;WAY-EKB 569) is an irreversible inhibitor of EGFR with an IC_{50} of 38.5 nM; also slightly inhibits Src, MEK/ERK and ErbB2 with IC_{50}s of 282, 800, and 1255 nM, respectively.

IC_{50} & Target

EGFR
38.5 nM (IC_{50})

In Vitro

Pelitini has much greater inhibitory activity against the EGFR kinase than against Src, MEK/ERK, Cdk4, c-Met, Raf and ErbB2, for example, the IC_{50} for EGFR is 32-fold lower than the IC_{50} for the closely related ErbB2. Pelitinib results in a dramatic reduction in EGFR phosphorylation but no change in the total amount of EGFR protein. It requires at least 10-fold more drug to equivalently inhibit ErbB2 phosphorylation in similar assays, and EKB-569 does not block phosphorylation of another

	receptor tyrosine kinase (c-Met) assessed in the same manner[1]. EKB-569 is a potent inhibitor of proliferation in NHEK, A431, and MDA-468 cells (IC_{50}=61, 125, and 260 nM, respectively) but not MCF-7 cells (IC_{50}=3600 nM). EKB-569 is also a potent inhibitor of EGF-induced phosphorylated EGF-R (pEGF-R) in A431 and NHEK cells (IC_{50}=20-80 nM)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	A single oral dose of 10 mg/kg EKB-569 inhibits EGFR phosphorylation in A431 xenografts within 60 minutes. Twenty-four hours later, EGFR activity is still inhibited by over 50% by this single oral dose. The half-life of EKB-569 in mouse plasma is about 2 hours[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	For experiments using cells in culture, A431 cells or 3T3/c-erbB-2 cells over-expressing c-erbB2 are are treated with various concentrations of EKB-569 for 2.75 h before co-incubation with 100 ng/mL EGF (A431 cells) or no growth factor (3T3/c-erbB-2 cells) for 0.25 h. Cells are ished twice with cold phosphate-buffered saline (PBS) before adding to lysis buffer for 20 min on ice, before immunoprecipitation and SDS–PAGE-immunoblotting[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: For in vivo experiments, athymic nu/nu female mice are implanted subcutaneously with 5×10^6 A431 tumor cells. When tumors reach a mass of 200-300 mg, animals are treated with a single dose of 10 mg/kg EKB-569 in pH 2.0 water per gavage. Tumors from control and drug-treated animals are excised and minced into 1-mm pieces for anlysis[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Harvard Medical School LINCS LIBRARY

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REFERENCES

[1]. Torrance CJ, et al. Combinatorial chemoprevention of intestinal neoplasia. Nat Med. 2000 Sep;6(9):1024-8.

[2]. Nunes M, et al. Phosphorylation of extracellular signal-regulated kinase 1 and 2, protein kinase B, and signal transducer and activator of transcription 3 are differently inhibited by an epidermal growth factor receptor inhibitor, EKB-569, in tumor cells and normal human keratinocytes. Mol Cancer Ther. 2004 Jan;3(1):21-7.

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