Mavelertinib

Cat. No.: HY-12972

CAS No.: 1776112-90-3

Molecular Formula: $C_{18}H_{22}FN_9O_2$

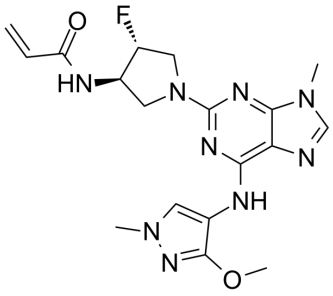
Molecular Weight: 415.42

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 : 47.5 mg/mL (114.34 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4072 mL	12.0360 mL	24.0720 mL
	5 mM	0.4814 mL	2.4072 mL	4.8144 mL
	10 mM	0.2407 mL	1.2036 mL	2.4072 mL

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

BIOLOGICAL ACTIVITY

Description

Mavelertinib is a selective, orally available and irreversible EGFR tyrosine kinase inhibitor (EGFR TKI), with IC_{50}s of 5, 4, 12 and 3 nM for Del, L858R, and double mutants T790M/L858R and T790M/Del, respectively. Mavelertinib can be used for the research of non-small-cell lung cancer (NSCLC)[1][2][3][4].

IC_{50} & Target

IC50: 3 nM (T790M/Del), 4 nM (L858R), 5 nM (Del), 12 nM (T790M/L858R), 307 nM (wild-type)[1]

In Vitro

Mavelertinib exhibits selectivity over wild-type EGFR (IC_{50}=307 nM)[1].
Mavelertinib (10 μM) exhibits less than 50% effect or inhibition against all nonkinase targets[1].
Mavelertinib inhibits the hERG26 current with an IC_{50} > 100 μM[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Mavelertinib exhibits low to moderate oral bioavailability (mouse 60%, rat 11%, dog 66%) following oral administration (mouse 1, rat 30, dog 3 mg/kg)[1].
Mavelertinib exhibits short plasma half-lives (mouse 0.56, rat 0.28, dog 1.3 h) due to moderate to high plasma clearance (mouse 53, rat 49, dog 12 mL/min/kg) and low steady-state volume of distribution (mouse 1.48, rat 0.66, dog 0.94 L/kg)

following intravenous administration (1 mg/kg to mouse, rat and dog)[1].

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

Animal Model:	Female Nu/Nu mice[1]
Dosage:	1 mg/kg (Pharmacokinetic Analysis)
Administration:	P.o. and i.v. administration
Result:	Oral bioavailability (60%), $T_{1/2}$ (1.48 h).

REFERENCES

[1]. Planken S, et, al. Discovery of N-((3R,4R)-4-Fluoro-1-(6-((3-methoxy-1-methyl-1H-pyrazol-4-yl)amino)-9-methyl-9H-purin-2-yl)pyrrolidine-3-yl)acrylamide (PF-06747775) through Structure-Based Drug Design: A High Affinity Irreversible Inhibitor Targeting Oncogenic EGFR Mutants with Selectivity over Wild-Type EGFR. J Med Chem. 2017 Apr 13;60(7):3002-3019.

[2]. Murtuza A, et, al. Novel Third-Generation EGFR Tyrosine Kinase Inhibitors and Strategies to Overcome Therapeutic Resistance in Lung Cancer. Cancer Res. 2019 Feb 15; 79(4): 689-698.

[3]. Patel H, et, al. Recent updates on third generation EGFR inhibitors and emergence of fourth generation EGFR inhibitors to combat C797S resistance. Eur J Med Chem. 2017 Dec 15; 142:32-47.

[4]. Husain H, et, al. First-in-human phase I study of PF-06747775, a third-generation mutant selective EGFR tyrosine kinase inhibitor (TKI) in metastatic EGFR mutant NSCLC after progression on a first-line EGFR TKI. Annals of Oncology. 2017 Sep.

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