Temuterkib

Cat. No.: HY-101494

CAS No.: 1951483-29-6

Molecular Formula: $C_{22}H_{27}N_7O_2S$

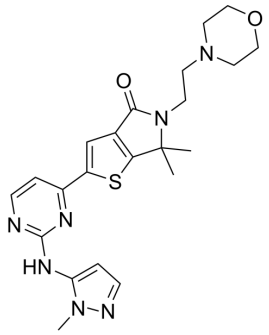
Molecular Weight: 453.56

Target: ERK

Pathway: MAPK/ERK Pathway; Stem Cell/Wnt

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 20 mg/mL (44.10 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2048 mL	11.0239 mL	22.0478 mL
5 mM	0.4410 mL	2.2048 mL	4.4096 mL
10 mM	0.2205 mL	1.1024 mL	2.2048 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 mg/mL (4.41 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2 mg/mL (4.41 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2 mg/mL (4.41 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Temuterkib (LY3214996) is a highly selective inhibitor of ERK1 and ERK2, with IC_{50} of 5 nM for both enzymes in biochemical assays. Temuterkib potently inhibits cellular p-RSK1 in BRAF and RAS mutant cancer cell lines. Temuterkib shows potent antitumor activities in cancer models with MAPK pathway alterations.

IC_{50} & Target

ERK1	ERK2
5 nM (IC_{50})	5 nM (IC_{50})

In Vitro	Temuterkib is a highly selective inhibitor of ERK1 and ERK2, with IC_{50} of 5 nM for both enzymes in biochemical assays. Temuterkib potently inhibits cellular phospho-RSK1 in BRAF and RAS mutant cancer cell lines. In an unbiased tumor cell panel sensitivity profiling for inhibition of cell proliferation, tumor cells with MAPK pathway alterations including BRAF, NRAS or KRAS mutation are generally sensitivity to Temuterkib[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	In tumor xenograft models, Temuterkib inhibits PD biomarker phospho-p90RSK1 in tumors and the PD effects are correlated with compound exposures and anti-tumor activities. Temuterkib shows either similar or superior anti-tumor activity as compared to other published ERK inhibitors in BRAF or RAS mutant cell lines and xenograft models. Oral administration of single-agent Temuterkib significantly inhibits tumor growth in vivo and is well tolerated in BRAF or NRAS mutant melanoma, BRAF or KRAS mutant colorectal, lung and pancreatic cancer xenografts or PDX models. Therefore, Temuterkib can be tailored for treatment of cancers with MAPK pathway alteration. In addition, Temuterkib has anti-tumor activity in a PLX4032-resistant A375 melanoma xenograft model due to MAPK reactivation, may have potential for treatment of melanoma patients who have failed BRAF therapies. More importantly, Temuterkib can be combined with investigational and approved agents in preclinical models, particularly KRAS mutant models. Combination treatment of Temuterkib and CDK4/6 inhibitor abemaciclib is well tolerated and results in potent tumor growth inhibition or regression in multiple in vivo cancer models, including KRAS mutant colorectal and non-small cell lung cancers[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Signal Transduct Target Ther. 2020 Sep 30;5(1):197.
- Mol Cell. 2019 Jan 3;73(1):7-21.e7.
- Theranostics. 2021 Mar 5;11(10):5045-5060.
- EMBO Mol Med. 2023 Jan 18;e16235.
- Cell Death Dis. 2022 Dec 27;13(12):1075.

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REFERENCES

[1]. Shripad V. Bhagwat, et al. Abstract 4973: Discovery of LY3214996, a selective and novel ERK1/2 inhibitor with potent antitumor activities in cancer models with MAPK pathway alterations. Cancer Research. July 2017.

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