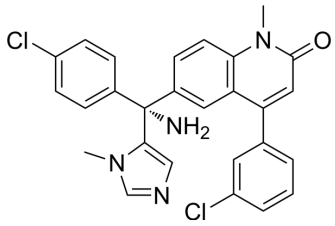
Tipifarnib

Cat. No.:	HY-10502
CAS No.:	192185-72-1
Molecular Formula:	$C_{27}H_{22}Cl_2N_4O$
Molecular Weight:	489.40
Target:	Farnesyl Transferase
Pathway:	Metabolic Enzyme/Protease
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 : 33.33 mg/mL (68.10 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0433 mL	10.2167 mL	20.4334 mL
	5 mM	0.4087 mL	2.0433 mL	4.0867 mL
	10 mM	0.2043 mL	1.0217 mL	2.0433 mL

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

In Vivo

1. Add each solvent one by one: 20% HP-β-CD/10 mM Citrate pH 2.0
   Solubility: 10 mg/mL (20.43 mM); Clear solution; Need ultrasonic and warming and heat to 60°C
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.11 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.11 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.11 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Tipifarnib (IND 58359) binds to and inhibits farnesyltransferase (FTase) with an IC_{50} of 0.86 nM. Antineoplastic activity and antiparasitic activity[1].

IC_{50} & Target

IC50: 0.86 nM (FTase)

In Vitro	Tipifarnib is a potent inhibitor of Trypanosoma Cruzi with the ED_{50} of 4 nM[1]. Tipifarnib inhibits isolated human farnesyltransferase for a lamin B peptide and for the K-RasB peptide with IC_{50} of 0.86 nM and 7.9 nM, respectively[2]. Tipifarnib shows inhibition of cell growth or angiogenesis, and induction of apoptosis in aggressive prostate cancer (PCa)[3]. Tipifarnib (0.25 μM, 1 μM; 48 h) shows a significant decrease in the concentration of exosomes in C4-2B cells and PC-3 cells[3]. Tipifarnib (1 μM) significantly inhibits the protein concentration of Alix, nSMase2, and Rab27a in C4-2B cells[3]. Tipifarnib (0.25 μM) significantly inhibits the activation of p-ERK (downstream effector molecule of the Ras/Raf/ERK signaling pathway) but not total ERK in C4-2B and PC-3 cells[3]. Tipifarnib (1.25-5 μM; 30 min) promotes endoplasmic reticulum stress in U937 cells, resulting in dysregulation of intracellular calcium homeostasis[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Tipifarnib (10 mg/kg; ip; single dose) upregulated antiapoptotic protein, Bcl-xL in liver, and prevents mosue death induced by GalN/LPS[5]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	GalN/LPS challenge mouse[5]
Dosage:	10 mg/kg; while chanllenge with GalN (400 mg/kg; IP) and LPS (32 g/kg)
Administration:	IP; 60 min before challenge
Result:	Protected primary hepatocytes from GalN/tumor necrosis factor-induced cell death. Inhibited caspase 3 activation and upregulating antiapoptotic proteins.

CUSTOMER VALIDATION

- Circ Res. 2024 Jun 7.
- Mol Cell. 2021 Jul 1;81(13):2736-2751.e8.
- Mol Cell. 2021 Oct 7;81(19):4076-4090.e8.
- J Immunother Cancer. 2022 Apr;10(4):e004399.
- Br J Cancer. 2024 Jan 26.

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REFERENCES

[1]. Devendra S Puntambekar, et al. Inhibition of farnesyltransferase: a rational approach to treat cancer? J Enzyme Inhib Med Chem. 2007 Apr;22(2):127-40.

[2]. End DW, et al. Characterization of the antitumor effects of the selective farnesyl protein transferase inhibitor R115777 in vivo and in vitro. Cancer Res. 2001 Jan 1;61(1):131-7

[3]. Amrita Datta, et al. High-throughput screening identified selective inhibitors of exosome biogenesis and secretion: A drug repurposing strategy for advanced cancer. Sci Rep. 2018 May 25;8(1):8161.

Caution: Product has not been fully validated for medical applications. For research use only.

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