SHP099 monohydrochloride

Cat. No.: HY-100388A

CAS No.: 2200214-93-1

Molecular Formula: $C_{16}H_{20}Cl_3N_5$

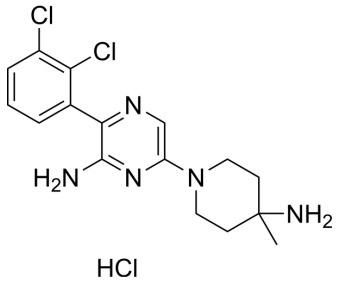
Molecular Weight: 388.72

Target: Phosphatase; SHP2

Pathway: Metabolic Enzyme/Protease; Protein Tyrosine Kinase/RTK

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 4.1 mg/mL (10.55 mM; Need ultrasonic and warming)

H_2O : ≥ 2.5 mg/mL (6.43 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5725 mL	12.8627 mL	25.7255 mL
	5 mM	0.5145 mL	2.5725 mL	5.1451 mL
	10 mM	0.2573 mL	1.2863 mL	2.5725 mL

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

In Vivo

1. Add each solvent one by one: 50% PEG300 >> 50% saline
   Solubility: 20 mg/mL (51.45 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.43 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SHP099 hydrochloride is a potent, selective and orally available SHP2 inhibitor with an IC_{50} of 70 nM[1].

IC_{50} & Target

IC50: 70 nM (SHP2)[1]

In Vitro

The X-ray co-crystal for SHP099 with SHP2 reveals a new interaction with the basic amine and the Phe113 backbone carbonyl. SHP099 shows inhibition of cell proliferation (KYSE-520 model) with an IC_{50} of 1.4 μM. SHP099 shows high solubility and high permeability with no apparent efflux in Caco-2 cells[1]. SHP099 concurrently binds to the interface of the N-terminal SH2, C-terminal SH2, and protein tyrosine phosphatase domains, thus inhibiting SHP2 activity through an allosteric mechanism. SHP099 suppresses RAS–ERK signalling to inhibit the proliferation of receptor-tyrosine-kinase-driven

	human cancer cells[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	After a single doses of 30 and 100 mg/kg , dose-dependent exposure and modulation of the pharmacodynamic marker p-ERK is observed in the xenografts. A daily oral dose of 10 or 30 mg/kg yield 19% and 61% tumor growth inhibition, respectively. Tumor stasis is achieved at 100 mg/kg[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	The inhibition of SHP2 from the tested compounds (SHP099) concentrations varying from 0.003-100 μM is monitored using an assay in which 0.5 nM of SHP2 is incubated with of 0.5 μM of peptide IRS1_pY1172(dPEG8)pY1222. After 30-60 minutes incubation at the surrogate substrate, DiFMUP is added to the reaction and incubated at 25 °C for 30 minutes. The reaction is then quenched by the addition of 5 μL of a 160 μM solution of bpV(Phen). The fluorescence signal is monitored using a microplate reader using excitation and emission wavelengths of 340 nm and 450 nm, respectively[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	Cells are plated onto 96-well plates in 100 μL medium. SHP099 with various concentrations (1.25, 2.5, 5, 10, 20 μM) are added 24 h after cell plating. At day 5, 50 μL Celltiter-Glo reagent is added, and the luminescent signal is determined[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Signal Transduct Target Ther. 2022 Sep 12;7(1):317.
- Nat Immunol. 2021 Oct 22.
- Cancer Discov. 2018 Oct;8(10):1237-1249.
- ACS Nano. 2023 Aug 14.
- Nat Commun. 2018 Oct 30;9(1):4507.

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REFERENCES

[1]. Garcia Fortanet J, et al. Allosteric Inhibition of SHP2: Identification of a Potent, Selective, and Orally Efficacious Phosphatase Inhibitor. J Med Chem. 2016 Sep 8;59(17):7773-82.

[2]. Chen YN, et al. Allosteric inhibition of SHP2 phosphatase inhibits cancers driven by receptor tyrosine kinases. Nature. 2016 Jul 7;535(7610):148-52.

[3]. Carmine Fedele, et al. SHP2 Inhibition Abrogates MEK inhibitor Resistance in Multiple Cancer Models. bioRxiv. April 25, 2018.

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