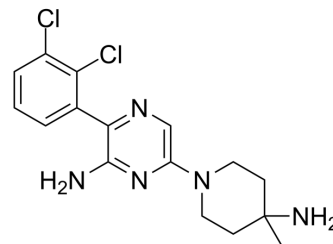


SHP099

Cat. No.:	HY-100388		
CAS No.:	1801747-42-1		
Molecular Formula:	C ₁₆ H ₁₉ Cl ₂ N ₅		
Molecular Weight:	352.26		
Target:	Phosphatase		
Pathway:	Metabolic Enzyme/Protease		
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 : 12 mg/mL (34.07 mM; Need ultrasonic)
 H₂O : 1 mg/mL (2.84 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	2.8388 mL	14.1941 mL	28.3881 mL
	5 mM	0.5678 mL	2.8388 mL	5.6776 mL
	10 mM	0.2839 mL	1.4194 mL	2.8388 mL

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

In Vivo

- Add each solvent one by one: 0.5% CMC-Na/saline water
Solubility: 10 mg/mL (28.39 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 1.2 mg/mL (3.41 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 1.2 mg/mL (3.41 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 1.2 mg/mL (3.41 mM); Clear solution
- Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
Solubility: ≥ 0.67 mg/mL (1.90 mM); Clear solution
- Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
Solubility: ≥ 0.67 mg/mL (1.90 mM); Clear solution
- Add each solvent one by one: 1% DMSO >> 99% saline
Solubility: ≥ 0.13 mg/mL (0.37 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	SHP099 is a potent, selective, orally available SHP2 inhibitor with an IC ₅₀ of 70 nM ^[1] .
IC₅₀ & Target	IC50: 70 nM (SHP2) ^[1]
In Vitro	<p>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 IC₅₀ 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].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
In Vivo	<p>After a single doses of 30 and 100 mg/kg (red and blue lines, respectively), 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].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

PROTOCOL

Kinase Assay ^[1]	<p>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 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].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
Cell Assay ^[1]	<p>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].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

CUSTOMER VALIDATION

- Cancer Discov. 2018 Oct;8(10):1237-1249.
- Nat Immunol. 2021 Oct 22.
- Hepatology. 2020 Jul;72(1):155-168.
- Hepatology. 2018 Jul;68(1):333-348.
- 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.

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

Tel: 609-228-6898

Fax: 609-228-5909

E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA