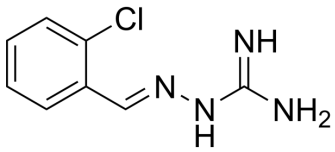
Icerguastat

Cat. No.:	HY-111022
CAS No.:	951441-04-6
Molecular Formula:	$C_8H_9ClN_4$
Molecular Weight:	196.64
Target:	Phosphatase
Pathway:	Metabolic Enzyme/Protease
Storage:	4°C, protect from light * In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (254.27 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	5.0854 mL	25.4272 mL	50.8544 mL
	5 mM	1.0171 mL	5.0854 mL	10.1709 mL
	10 mM	0.5085 mL	2.5427 mL	5.0854 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: ≥ 2.08 mg/mL (10.58 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (10.58 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Icerguastat (Sephin1), a derivative of Guanabenz lacking the α2-adrenergic activity, is a selective inhibitor of the phosphatase regulatory subunit PPP1R15A (R15A). Icerguastat inhibits eIF2α dephosphorylation, thereby prolonging the protective response. Anti-prion effect[1][2][3].

In Vitro

Icerguastat (5 μM) prolongs eIF2α phosphorylation in oligodendrocytes under stress[1].
Icerguastat (Sephin1) (selective inhibitor of a holophosphatase), safely and selectively inhibits a regulatory subunit of protein phosphatase 1 in vivo. Icerguastat selectively binds and inhibits the stress-induced PPP1R15A, but not the related and constitutive PPP1R15B, to prolong the benefit of an adaptive phospho-signaling pathway, protecting cells from otherwise lethal protein misfolding stress[2].

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

In Vivo

Icerguastat (4-8 mg/kg; i.p.; daily for 35 days) delays the onset of EAE (experimental autoimmune encephalomyelitis)[1].
Icerguastat (100 μg; i.p.) prolongs the survival of prion-infected mice[3].

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

Animal Model:	C57BL/6J female mice immunized with MOG35-55/CFA to induce chronic EAE[1]
Dosage:	4 mg/kg, 8 mg/kg
Administration:	I.p.; daily for 35 days
Result:	Significantly delayed clinical disease onset with both dosages, but to a greater extent with the 8 mg/kg treatment.

Animal Model:	Five-week-old female FVB mice (intracerebrally with mouse-adapted RML prions)[3]
Dosage:	100 μg
Administration:	I.p.; 3 times per week for 60 days, after 60 days of treatment, the treatment was reduced to two i.p. injections per week for another 20 days.
Result:	Significantly prolonged survival of prion-infected mice.

REFERENCES

[1]. Chen Y, et al. Sephin1, which prolongs the integrated stress response, is a promising therapeutic for multiple sclerosis. Brain. 2019;142(2):344-361.

[2]. Das I, et al. Preventing proteostasis diseases by selective inhibition of a phosphatase regulatory subunit. Science. 2015;348(6231):239-242.

[3]. Thapa S, et al. Sephin1 Reduces Prion Infection in Prion-Infected Cells and Animal Model. Mol Neurobiol. 2020;57(5):2206-2219.

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