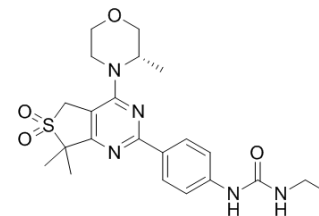


CZ415

Cat. No.:	HY-100222		
CAS No.:	1429639-50-8		
Molecular Formula:	C ₂₂ H ₂₉ N ₅ O ₄ S		
Molecular Weight:	459.56		
Target:	mTOR		
Pathway:	PI3K/Akt/mTOR		
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 : 100 mg/mL (217.60 mM; Need ultrasonic)			
		Solvent Concentration	Mass	
			1 mg	5 mg
			10 mg	
Preparing Stock Solutions	1 mM	2.1760 mL	10.8800 mL	21.7599 mL
	5 mM	0.4352 mL	2.1760 mL	4.3520 mL
	10 mM	0.2176 mL	1.0880 mL	2.1760 mL
Please refer to the solubility information to select the appropriate solvent.				
In Vivo	<ol style="list-style-type: none"> Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: ≥ 2.5 mg/mL (5.44 mM); Clear solution Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (5.44 mM); Clear solution Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (5.44 mM); Clear solution 			

BIOLOGICAL ACTIVITY

Description	CZ415 is a potent and highly selective mTOR inhibitor with a pIC ₅₀ of 8.07. CZ415 inhibits mTORC1 and mTORC2 protein complex.		
IC ₅₀ & Target	mTOR 8.07 (pIC ₅₀)	mTORC1	mTORC2
In Vitro	Inhibition of phosphorylation for both downstream targets results in 14.5 nM IC ₅₀ for pS6RP and 14.8 nM for pAKT. The		

immunosuppressive effect of CZ415 is measured by detecting secreted IFN γ after 18 hours in stimulated human whole blood and the resulting IC₅₀ is 226 nM. As a predictor for cardiotoxicity, the activity of CZ415 against the human cardiac ion channel hERG is assessed in a whole-cell patch-clamp assay in HEK293 cells resulting in an IC₅₀ of 48 μ M^[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

CZ415 is a highly selective mTOR inhibitor showing in vivo efficacy in a collagen induced arthritis (CIA) model. For full characterization of CZ415 and to enable improved dose predictions, the pharmacokinetic (PK) profile is assessed in rat. PK and oral bioavailability are determined after of 1 mg/kg intravenous (iv) bolus and 3 mg/kg oral (po) administration. The observed plasma clearance, corresponding to 45% liver blood flow, suggests that sufficient levels of free compound are circulating in the animal over time. The oral uptake is rapid with a T_{max} of 0.5 h and bioavailability F = 44% indicates very good absorption from the gut^[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration ^[1]

Mice^[1]

To determine the effects of CZ415 on its pharmacological target, dose-dependent changes in phosphorylation levels of S6 Ribosomal Protein and Akt - both downstream targets of mTOR are assessed. CZ415 is administered orally at 1, 3 and 10 mg/kg to mice 1 h before anti-CD3 stimulus. 15 min after stimulation, spleens are dissected and analyzed for pS6RP and pAKT levels. A dose related significant inhibition of phosphorylation of both S6RP and Akt are observed after compound administration. In particular, 1 and 3 mg/kg CZ415 could fully inhibit S6RP phosphorylation induced by anti-CD3 stimulation and 10 mg/kg additionally decreased the constitutive phosphorylation levels as measured in the control group. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Front Pharmacol. 2020, 11:580407.
- Acta Trop. 2020 Dec;212:105708.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Cansfield AD, et al. CZ415, a Highly Selective mTOR Inhibitor Showing in Vivo Efficacy in a Collagen Induced Arthritis Model. ACS Med Chem Lett. 2016 Jun 10;7(8):768-73.

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