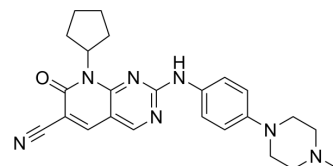


Narazaciclib

Cat. No.:	HY-12624
CAS No.:	1357470-29-1
Molecular Formula:	C ₂₄ H ₂₇ N ₇ O
Molecular Weight:	429.52
Target:	CDK; AMPK; PDGFR
Pathway:	Cell Cycle/DNA Damage; Epigenetics; PI3K/Akt/mTOR; Protein Tyrosine Kinase/RTK
Storage:	<div> <div>Powder</div> <div>-20°C</div> <div>3 years</div> </div> <div> <div></div> <div>4°C</div> <div>2 years</div> </div> <div> <div>In solvent</div> <div>-80°C</div> <div>6 months</div> </div> <div> <div></div> <div>-20°C</div> <div>1 month</div> </div>



SOLVENT & SOLUBILITY

In Vitro	DMSO : 16.67 mg/mL (38.81 mM); ultrasonic and warming and heat to 60°C)				
	Preparing Stock Solutions	<div>Solvent Concentration</div> <div>Mass</div>	1 mg	5 mg	10 mg
			1 mM	2.3282 mL	11.6409 mL
		5 mM	0.4656 mL	2.3282 mL	4.6564 mL
		10 mM	0.2328 mL	1.1641 mL	2.3282 mL
	Please refer to the solubility information to select the appropriate solvent.				
In Vivo	1. Add each solvent one by one: 0.5% CMC-Na/saline water Solubility: 5 mg/mL (11.64 mM); Suspended solution; Need ultrasonic				

BIOLOGICAL ACTIVITY

Description	Narazaciclib (ON123300), a strong and brain-penetrant ^[1] multi-kinase inhibitor, inhibits CDK4 (IC ₅₀ =3.9 nM), Ark5 (IC ₅₀ =5 nM), PDGFRβ (IC ₅₀ =26 nM), FGFR1 (IC ₅₀ =26 nM), RET (IC ₅₀ =9.2 nM), and FYN (IC ₅₀ =11 nM). Single agent Narazaciclib causes a dose-dependent suppression of phosphorylation of Akt as well as activation of Erk in brain tumors ^[2] . Narazaciclib inhibits CDK6 with an IC ₅₀ of 9.82 nM ^[3] .			
IC ₅₀ & Target	Cdk4/cyclin D1 3.9 nM (IC ₅₀)	ARK5 5 nM (IC ₅₀)	CDK6/cyclinD1 9.82 nM (IC ₅₀)	RET 9.2 nM (IC ₅₀)
	FYN 11 nM (IC ₅₀)	FGFR1 26 nM (IC ₅₀)	PDGFRβ 26 nM (IC ₅₀)	PI3K-δ 144 nM (IC ₅₀)
In Vitro	Narazaciclib (ON123300) inhibits U87 glioma cell proliferation with an IC ₅₀ of 3.4±0.1 μM ^[2] . Narazaciclib (1 and 10 μM)			

inhibits cell proliferation in a panel of 11 glioma models including a patient-derived model (GBM10)^[2]. Narazacilib (6.3 μ M; 1 h) reduces phosphorylation of Akt and its downstream signaling components, P70S6K, 40S rpS6 and Rb S780, yet ON123300 induces Erk activation in U87 cells; both in a dose- and time-dependent manner^[2]. ON123300 inhibits PI3K δ with the IC₅₀ of 144nM^[3].

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

Cell Cytotoxicity Assay^[2]

Cell Line:	U87 glioma cells
Concentration:	0, 4, 8, 12, 16 μ M
Incubation Time:	72 hour
Result:	Had an IC ₅₀ equal to 3.4 \pm 0.1 μ M.

Western Blot Analysis^[2]

Cell Line:	U87 cells
Concentration:	6.3 μ M
Incubation Time:	1 h
Result:	Inhibited phosphorylation of Akt (at S473 site) and its downstream signaling components, P70S6K, 40S ribosomal protein S6 (rpS6) and Rb S780 (decreased to 40.1%; 31.8 %; 60.5%; 54.5% relatively to control), yet increased p-Erk (increased to 120% relative to control).

In Vivo

Narazacilib (ON123300) decreases p-Akt expression and increases p-Erk activity in brain tumors upon administration at both IV doses of 5 mg/kg and 25 mg/kg in U87 brain tumor-bearing mouse. The half-life ($T_{1/2}$) is 1.5 h for 5 mg/kg and 25 mg/kg in plasma^[2].

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

Animal Model:	NIH Swiss nude mice bearing U87 glioma model ^[2] .
Dosage:	5 mg/kg or 25 mg/kg
Administration:	IV bolus at a dose of either 5 mg/kg or 25 mg/kg via a tail vein.
Result:	The p-Akt rapidly declined and reached nadir values of 73% and 60% of control within 30 min after 5 mg/kg and 25 mg/kg dose levels, respectively.

CUSTOMER VALIDATION

- Autophagy. 2021 Jun;17(6):1426-1447.
- Department of Biochemistry. 2020 Oct.

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REFERENCES

- [1]. Hua Lv, et al. Integrated pharmacokinetic-driven approach to screen candidate anticancer drugs for brain tumor chemotherapy. AAPS J. 2013 Jan;15(1):250-7.

[2]. Xiaoping Zhang, et al. Preclinical pharmacological evaluation of a novel multiple kinase inhibitor, ON123300, in brain tumor models. Mol Cancer Ther. 2014 May;13(5):1105-16.

[3]. S K A Divakar, et al. Dual inhibition of CDK4/Rb and PI3K/AKT/mTOR pathways by ON123300 induces synthetic lethality in mantle cell lymphomas. Leukemia. 2016 Jan;30(1):86-93.

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

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