# Narazaciclib

**Cat. No.:** HY-12624

**CAS No.:** 1357470-29-1

**Molecular Formula:** $C_{24}H_{27}N_7O$

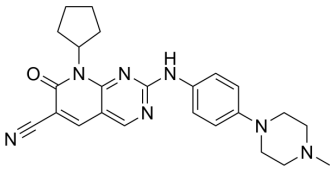
**Molecular Weight:** 429.52

**Target:** CDK; AMPK; PDGFR

**Pathway:** Cell Cycle/DNA Damage; Epigenetics; PI3K/Akt/mTOR; Protein Tyrosine Kinase/RTK

**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 : 16.67 mg/mL (38.81 mM; ultrasonic and warming and heat to 60°C)

| Preparing Stock Solutions | Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 2.3282 mL | 11.6409 mL | 23.2818 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<br>3.9 nM ($IC_{50}$) | ARK5<br>5 nM ($IC_{50}$) | CDK6/cyclinD1<br>9.82 nM ($IC_{50}$) | RET<br>9.2 nM ($IC_{50}$) |
| FYN<br>11 nM ($IC_{50}$) | FGFR1<br>26 nM ($IC_{50}$) | PDGFRβ<br>26 nM ($IC_{50}$) | PI3K-δ<br>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].
Narazaciclib (6.3 μM; 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 PI3Kδ with the $IC_{50}$ 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 μM |
| Incubation Time: | 72 hour |
| Result: | Had an $IC_{50}$ equal to 3.4±0.1 μM. |

Western Blot Analysis[2]

| | |
|---|---|
| Cell Line: | U87 cells |
| Concentration: | 6.3 μM |
| 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**

Narazaciclib (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].

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| | |
|---|---|
| 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.

See more customer validations on www.MedChemExpress.com

## 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.



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