# IC-87114

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| **Cat. No.:** | HY-10110 |
| **CAS No.:** | 371242-69-2 |
| **Molecular Formula:** | $C_{22}H_{19}N_7O$ |
| **Molecular Weight:** | 397.43 |
| **Target:** | PI3K |
| **Pathway:** | PI3K/Akt/mTOR |

**Storage:**

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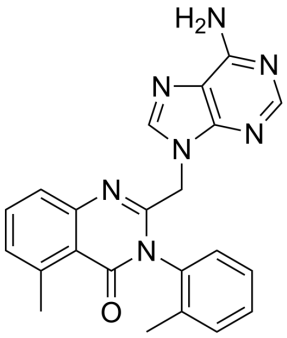
|---|---|---|
| Powder | -20°C | 3 years |
| | 4°C | 2 years |
| In solvent | -80°C | 2 years |
| | -20°C | 1 year |



## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : 10 mg/mL (25.16 mM; Need ultrasonic)

| Preparing Stock Solutions | Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 2.5162 mL | 12.5808 mL | 25.1617 mL |
| | 5 mM | 0.5032 mL | 2.5162 mL | 5.0323 mL |
| | 10 mM | 0.2516 mL | 1.2581 mL | 2.5162 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: ≥ 1 mg/mL (2.52 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1 mg/mL (2.52 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1 mg/mL (2.52 mM); Clear solution

## BIOLOGICAL ACTIVITY

**Description**

IC-87114 is a potent and selective PI3Kδ inhibitor with $IC_{50}$ of 0.5 μM.

**$IC_{50}$ & Target**

| PI3Kδ | PI3Kγ | PI3Kβ |
|---|---|---|
| 0.5 μM ($IC_{50}$) | 29 μM ($IC_{50}$) | 75 μM ($IC_{50}$) |

**In Vitro**

IC-87114 (IC87114), an analog of the original inhibitor, is synthesized and tested for PI3Kδ selectivity relative to the other class I PI3Ks. The $IC_{50}$ of IC87114 for PI3Kδ inhibition is 0.5 μM whereas the $IC_{50}$ values for PI3Kα, PI3Kβ, and PI3Kγ are >100,

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| | 75, and 29 μM, respectively. Thus IC87114 is 58-fold more selective for PI3Kδ relative to PI3Kγ, and over 100-fold selective relative to PI3Kα and PI3Kβ. IC87114 selectively antagonizes PI3Kδ over at least a concentration range of 0.3-10 μM[1]. IC-87114 (10 μM) is also used to selectively inhibit PI3Kδ catalytic activity to address this question. IC87114 (10 μM) effectively inactivates Akt in macrophages after treatment for 1 hour (n=6; P<0.001 versus control). The effect of IC-87114 (IC87114) is next detected ton AP-1 DNA-binding activity. The electrophoretic mobility shift assay assay demonstrates that DNA-binding activity of AP-1 is significantly increased after the treatment with TNF-α (10 ng/mL; P<0.001) and TNF-α (20 ng/mL; P<0.001). IC87114 alone induces AP-1 DNA-binding activity after treatment for 1 hour. Furthermore, there is stronger AP-1 DNA-binding activity after costimulation of IC87114 (10 μM) and TNF-α (0-20 ng/mL) than only treatment with TNF-α (0-20 ng/mL; n=5; P<0.01). IC87114 (10 μM) also effectively inhibits p110δ catalytic activities (Akt phosphorylation) in macrophages with or without TNF-α treatment for 24 hours (n=6; P<0.001)[2].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| **In Vivo** | Treatment with PD 89059 (10 mg/kg), IC-87114 (0.3 mg/kg) and BAY 11-7085 (10 mg/kg), significantly (P<0.05) reduces the OVA- induced inflammatory cell influx into the airways and the histopathological airway remodeling. However, these treatments does not significantly improve OVA induced-AHR (P>0.05). Of note, the observed reduction in the histopathological airway remodeling induced by PD 89059, IC-87114 and BAY 11-7085 are less effective as compared to the reduction seen with AG 1478 and SU6656[3].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

## PROTOCOL

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| **Cell Assay** [2] | The murine macrophage cell line RAW264.7 and peritoneal macrophages from both types of mice are maintained in Dulbecco's modified Eagle's medium (DMEM) with 10% fetal calf serum (FCS). Cultures are maintained at 37°C in a humidified incubator in a 95% $O_2$ plus 5% $CO_2$ atmosphere. Cells are treated with varied concentrations of TNF-α and used IC-87114 (IC87114) to inhibit PtdIns(3,4,5)P3-dependent phosphorylation of Akt before TNF-α stimulation at early time points (30 min)[2].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| **Animal Administration** [3] | Mice[3]<br>BALB/c mice are immunized once by i.p. injection of 10 μg ovalbumin (OVA) in 0.2 ml of alu-Gel-S on day 0. Ten days later, mice are intranasally (i.n.) challenged with OVA (30 μg in 50 μL PBS) or PBS, once daily, over four consecutive days. To investigate if ERK1/2, PI3Kδ and NF-κB are signaling effectors downstream of EGFR transactivation, six treatment groups (A-F, 10-30 animals per group) are established. Mice in groups A and B are pretreated intranasally with 0.2 mL of the vehicle for the drugs. Groups C, D and E are pretreated with the same volume of three different drugs (PD 98059, IC-87114 and BAY 11-7085, respectively) at 10 mg/kg, 10 mg/kg and 0.3 mg/kg respectively, and group F with Dexamethasone (1 mg/kg), 1 h before each i.n. challenge with OVA. These doses are chosen from previous studies where they are shown to be effective.<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

## CUSTOMER VALIDATION

- Sci Signal. 2021 Dec 21;14(714):eabj0057.
- Int J Chron Obstruct Pulmon Dis. 2023 May 6 ,18, 797—809.

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## REFERENCES

[1]. Sadhu C, et al. Essential role of phosphoinositide 3-kinase delta in neutrophil directional movement. J Immunol. 2003 Mar 1;170(5):2647-54.

[2]. Zheng L, et al. Inactivation of PI3Kδ induces vascular injury and promotes aneurysm development by upregulating the AP-1/MMP-12 pathway in macrophages. Arterioscler Thromb Vasc Biol. 2015 Feb;35(2):368-77.

[3]. El-Hashim AZ, et al. Src-dependent EGFR transactivation regulates lung inflammation via downstream signaling involving ERK1/2, PI3Kδ/Akt and NFκB induction in a murine asthma model. Sci Rep. 2017 Aug 30;7(1):9919.



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