Product Data Sheet

# Midostaurin (PKC412)

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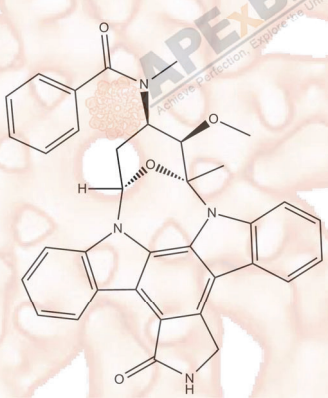
| **Cat. No.:** | B3709 |
| **CAS No.:** | 120685-11-2 |
| **Formula:** | C35H30N4O4 |
| **M.Wt:** | 570.64 |
| **Synonyms:** | |
| **Target:** | TGF-β / Smad Signaling |
| **Pathway:** | PKC |
| **Storage:** | Store at -20°C |



## Solvent & Solubility

In Vitro

≥57.1mg/mL in DMSO with ultrasonic

Preparing Stock Solutions

| Mass / Solvent / Concentration | 1mg | 5mg | 10mg |
|---|---|---|---|
| **1 mM** | 1.7524 mL | 8.7621 mL | 17.5242 mL |
| **5 mM** | 0.3505 mL | 1.7524 mL | 3.5048 mL |
| **10 mM** | 0.1752 mL | 0.8762 mL | 1.7524 mL |

Please refer to the solubility information to select the appropriate solvent.

## Biological Activity

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| Shortsummary | PKC inhibitor |
| $IC_{50}$ & Target | 22 nM (PKCα), 1 μM (VEGFR) |

In Vitro

**Cell Viability Assay**

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| Cell Line: | Ba/F3-FLT3-ITD cells, Ba/F3 cells, M0-91 and IMS-M2 cells |
| Preparation method： | The solubility of this compound in DMSO is > 10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months. |
| Reacting conditions: | 0.01–1 μM, 24–72 hr |
| Applications: | PKC412 showed a broad antiproliferative activity against various tumor and |

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| | | normal cell lines in vitro, and was able to reverse the Pgp-mediated multidrug resistance of tumor cells. PKC412 resulted in a dose-dependent increase in the G2/M phase of the cell cycle concomitant with increased polyploidy, apoptosis and enhanced sensitivity to ionizing radiation. PKC412 inhibited the proliferation of Ba/F3-FLT3-ITD cells with an IC50 of less than 10 nM within 24–72 hr, and was nontoxic toward parental Ba/F3 cells at concentrations up to 100 nM. PKC412 inhibited proliferation and viability of Ba/F3-FLT3-D835Y cells. PKC412 (0.01–1 μM, 15 min) potently inhibited FLT3 tyrosine phosphorylation in Ba/F3-FLT3-ITD and Ba/F3-FLT3-D835Y cells. In Ba/F3-FLT3-ITD cells, treatment with PKC412 (up to 0.04 μM) over a span of two months generated a polyclonal subline of Ba/F3-FLT3-ITD cells less sensitive to PKC412. PKC412 inhibited EN fusion tyrosine kinase in hematopoietic Ba/F3 cells. PKC412 significantly inhibited EN phosphorylation in M0-91 and IMS-M2 cells in a dose-dependent manner. |
| In Vivo | **Animal experiment** | |
| | Animal models: | Balb/c mice with FLT3/ITD-induced myeloproliferative disorder (MPD) |
| | Dosage form: | Oral administration, 100 mg/kg |
| | Applications: | Combination of PKC412 with loco-regional ionizing irradiation showed significant antitumor activity against tumors which are resistant to both ionizing radiation and chemotherapeutic agents (dysfunctional p53). Orally administered PKC412 strongly inhibited retinal neovascularization as well as laser-induced choroidal neovascularization in murine models. In Balb/c mice with FLT3/ITD-induced myeloproliferative disorder (MPD), PKC412 prolonged survival. PKC412 inhibited FLT3-ITD-mediated transformation. PKC412-treated mice displayed only a slight increase in mean spleen weight (80 mg). PKC412 (25 mg/kg, i.p.) protected cultured A549 cells that expressed mutant or wild-type K18 and mouse livers of the K18 Arg90Cys-overexpressing transgenic mice from Fas-induced apoptosis. |
| | Other notes: | Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal. |

## Product Citations

**See more customer validations on www.apexbt.com.**

## References

[1]. Fabbro D, Ruetz S, Bodis S, et al. PKC412-a protein kinase inhibitor with a broad therapeutic potential[J]. Anti-cancer drug design, 2000, 15(1): 17-28.
[2]. Weisberg E, Boulton C, Kelly L M, et al. Inhibition of mutant FLT3 receptors in leukemia cells by the small molecule tyrosine kinase inhibitor PKC412[J]. Cancer cell, 2002, 1(5): 433-443.
[3]. Chi HT, et al. ETV6-NTRK3 as a therapeutic target of small molecule inhibitor PKC412. Biochem Biophys Res Commun. 2012 Dec 7;429(1-2):87-92.
[4]. Juarez JC, et al. Copper binding by tetrathiomolybdate attenuates angiogenesis and tumor cell proliferation through the inhibition of superoxide dismutase 1. Clin Cancer Res. 2006 Aug 15;12(16):4974-82.

## Caution

**FOR RESEARCH PURPOSES ONLY.**

**NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.**

*Specific storage and handling information for each product is indicated on the product datasheet. Most APExBIO products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.*

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