# Ocifisertib fumarate

**Cat. No.:** HY-12300B

**CAS No.:** 1616420-30-4

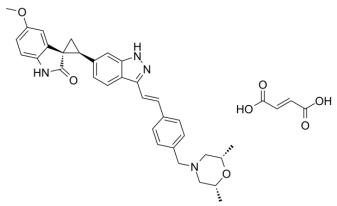
**Molecular Formula:** $C_{37}H_{38}N_4O_7$

**Molecular Weight:** 650.72

**Target:** Polo-like Kinase (PLK)

**Pathway:** Cell Cycle/DNA Damage

**Storage:** 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : 50 mg/mL (76.84 mM; Need ultrasonic)
$H_2O$ : 0.5 mg/mL (0.77 mM; Need ultrasonic and warming)

**Preparing Stock Solutions**

| Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|
| 1 mM | 1.5368 mL | 7.6838 mL | 15.3676 mL |
| 5 mM | 0.3074 mL | 1.5368 mL | 3.0735 mL |
| 10 mM | 0.1537 mL | 0.7684 mL | 1.5368 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: ≥ 2.5 mg/mL (3.84 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (3.84 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 2.5 mg/mL (3.84 mM); Clear solution; Need warming

## BIOLOGICAL ACTIVITY

**Description**

CFI-400945 fumarate is a potent, selective and orally bioavailable PLK4 inhibitor with a $K_i$ and an $IC_{50}$ of 0.26 nM and 2.8 nM, respectively.

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

| | | | |
|---|---|---|---|
| PLK4<br>2.8 nM ($IC_{50}$) | AURKA<br>140 nM ($IC_{50}$) | AURKB/INCENP<br>98 nM ($IC_{50}$) | TIE2/TEK<br>22 nM ($IC_{50}$) |
| TRKA<br>6 nM ($IC_{50}$) | TRKB<br>9 nM ($IC_{50}$) | | |

| | |
|---|---|
| **In Vitro** | CFI-400945 (compound 48) shows potent inhibitory activities against a panel of kinases, including PLK4, TRKA, TRKB, AURKA, AURKB/INCENP, and TIE2/TEK, with $IC_{50}$s of 2.8, 6, 9, 140, 98, 22 nM, and $EC_{50}$s of 12, 84, 88, 510, 102, 117 nM, respectively. CFI-400945 exhibits growth inhibition effects on breast, lung, ovarian and colon cancer cells. The $IC_{50}$s (in μM) are as follows: SKBr-3 (5.3), Cal-51 (0.26), BT-20 (0.058), A549 (0.005), OVCAR-3 (0.018), SW620 (0.38), Colo-205 (0.017), and HCT116+/+ (0.004) [1]. CFI-400945 inhibits autophosphorylation of PLK4 at serine 305 with an $EC_{50}$ value of 12.3 nM in cells overexpressing PLK4. Cancer cells treated with CFI-400945 exhibit effects consistent with PLK4 kinase inhibition, including dysregulated centriole duplication, mitotic defects, and cell death[2].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| **In Vivo** | Oral administration of CFI-400945 (3.0, 9.4 mg/kg) to mice bearing human cancer xenografts results in the significant inhibition of tumor growth at doses that are well tolerated. Increased antitumor activity is observed in PTEN-deficient compared to PTEN wild-type cancer xenografts. The maximum tolerated dose for once-daily administration of CFI-400945 is estimated to be 7.5-9.5 mg/kg[2].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

## PROTOCOL

| | |
|---|---|
| **Kinase Assay** [1] | Active PLK4 is purified and used to measure PLK4 activity, using an indirect ELISA detection system. PLK1, PLK2, PLK3, AURKA, and AUKB/INCENP compound inhibition are determined using FRET-based homogeneous assay kits from Invitrogen. The assays are performed with ATP concentrations of 25, 60, and 80 μM, respectively, for PLK1, PLK2, and PLK3 and ATP concentrations of 20 and 128 μM, respectively, for AURKA and AURKB/INCENP[1].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| **Cell Assay** [2] | MDA-MB-468, MCF-7, HCC1954, MDA-MB-231, SKBr-3, Cal-51, and BT-20 breast cancer cells are treated with 10 nM to 50 μM CFI-400945 for 5 days. Cell viability is measured using SRB assay[2].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| **Animal Administration** [2] | Mice: To treat an established tumor, CFI-400945 and the vehicle (water) are administered by oral gavage (2.5-20 mg/kg), and 5-FU and carboplatin are administered by intraperitoneal injection to mice as described in the text. Animal weights are monitored daily, and tumor volume is measured three times per week[2].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |



## CUSTOMER VALIDATION

- Nat Nanotechnol. 2021 Jul;16(7):830-839.
- Int J Mol Med. 2021 Jan;47(1):151-160.
- J Cancer Res Clin Oncol. 2020 Nov;146(11):2871-2883.
- Ir J Med Sci. 2022 May 4.

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## REFERENCES

[1]. Sampson PB, et al. The discovery of Polo-like kinase 4 inhibitors: identification of (1R,2S).2-(3-((E).4-(((cis).2,6-dimethylmorpholino)methyl)styryl). 1H.indazol-6-yl)-5'-methoxyspiro[cyclopropane-1,3'-indolin]-2'-one (CFI-400945) as a potent, orally active antitumor agent. J Med Chem. 2015 Jan 8;58(1):147-69.

[2]. Mason JM, et al. Functional characterization of CFI-400945, a Polo-like kinase 4 inhibitor, as a potential anticancer agent. Cancer Cell. 2014 Aug 11;26(2):163-76.