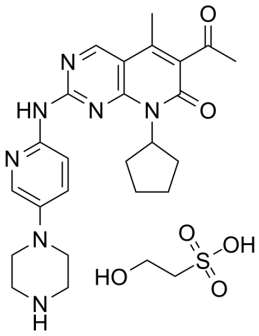
Palbociclib isethionate

Cat. No.:	HY-A0065
CAS No.:	827022-33-3
Molecular Formula:	$C_{26}H_{35}N_7O_6S$
Molecular Weight:	573.66
Target:	CDK
Pathway:	Cell Cycle/DNA Damage
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 1 year; -20°C, 6 months (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

H_2O : 50 mg/mL (87.16 mM; Need ultrasonic)
DMSO : 10 mg/mL (17.43 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.7432 mL	8.7160 mL	17.4319 mL
5 mM	0.3486 mL	1.7432 mL	3.4864 mL
10 mM	0.1743 mL	0.8716 mL	1.7432 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1 mg/mL (1.74 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Palbociclib (PD 0332991) isethionate is an orally active selective CDK4 and CDK6 inhibitor with IC_{50} values of 11 and 16 nM, respectively. Palbociclib isethionate has potent anti-proliferative activity and induces cell cycle arrest in cancer cells, which can be used in the research of HR-positive and HER2-negative breast cancer and hepatocellular carcinoma[1][3][4].

IC_{50} & Target

Cdk4/cyclin D3 9 nM (IC_{50})	Cdk4/cyclin D1 11 nM (IC_{50})	Cdk6/cyclin D2 16 nM (IC_{50})	DYRK1A 2000 nM (IC_{50})
MAPK 8000 nM (IC_{50})			

In Vitro

Palbociclib dihydrochloride (0-1 μM, 24 h) inhibits Rb Phosphorylation at Ser^{795} in MDA-MB-435 cells with an IC_{50} value of 0.063 μM, and obtains similar effects on both Ser^{780} and Ser^{795} phosphorylation in the Colo-205 colon carcinoma[1].
Palbociclib dihydrochloride (0-10 μM, 24 h) arrests MDA-MB-453 cells exclusively in G1 phase[1].

Palbociclib dihydrochloride (500 nM, 7 days) increases expression of homologous genes (H2d1, H2k1, and B2m) in MDA-MB-453 and MDA-MB-361 cells[2].
Palbociclib dihydrochloride (0-1 μM, 6 days) inhibits growth of several luminal ER-positive as well as HER2-amplified breast cancer cell lines, with IC_{50} values ranging from 4 nM to 1 μM[3].
Palbociclib dihydrochloride (0-1 μM, 3 days) inhibits the proliferation of human liver cancer cell lines with IC_{50} values ranging from 0.01 μM to 3.49 μM, and induces a reversible cell cycle arrest[4].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Cycle Analysis[1]

Cell Line:	MDA-MB-453 cells
Concentration:	0-1 μM
Incubation Time:	24 h
Result:	Arrested MDA-MB-453 cells in G1.

Cell Proliferation Assay[3]

Cell Line:	ER-positive as well as HER2-amplified breast cancer cell lines (MDA-MB-175, ZR-75-30, CAMA-1, etc.)
Concentration:	0-10 μM
Incubation Time:	6 days
Result:	Inhibited growth of luminal ER-positive as well as HER2-amplified breast cancer cell lines.

In Vivo

Palbociclib isethionate (oral adminstration, 75 or 150 mg/kg, daily for 14 days) produces rapid tumor regressions and delays tumor growth[1].
Palbociclib isethionate (oral adminstration, 90 mg/kg, daily for 12 days) reduces Treg numbers and the Treg:CD8 ratio in the spleen and lymph nodes in tumor-free mice, demonstrating the tumor-independent effects[2].
Palbociclib isethionate (oral administration, 100 mg/kg, daily for 1 week) has potent antitumour effects in genetically engineered mosaic mouse model of liver cancer[4].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Mice bearing Colo-205 colon carcinoma xenografts (p16 deleted)[1]
Dosage:	75, 150 mg/kg, daily for 14 days
Administration:	Oral adminstration
Result:	Produced rapid tumor regressions and a corresponding tumor growth delay of ~50 days.

Animal Model:	Tumor-free female FVB mice[2]
Dosage:	90 mg/kg (diluted in 50 nM sodium D-lactate), daily for 12 days
Administration:	Oral adminstration
Result:	Reduced total thymic mass and immature $CD4^+$ and $CD8^+$ double-positive thymocytes, and increased the fractions of $CD4^+$ and $CD8^+$ single-positive thymocytes.

Animal Model:	Genetically engineered mosaic mouse model of liver cancer (Myc;p53-sgRNA)[4]

Dosage:	100 mg/kg, daily for 1 week.
Administration:	Oral adminstration
Result:	Decreased the luminescence signal in liver and delayed tumour growth.

CUSTOMER VALIDATION

- Nature. 2020 Dec;588(7836):169-173.
- Nature. 2020 Jul;583(7817):620-624.
- Nature. 2017 Aug 24;548(7668):471-475.
- Nature. 2017 Jun 15;546(7658):426-430.
- Cancer Cell. 2017 Apr 10;31(4):576-590.e8.

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REFERENCES

[1]. Fry DW, et al. Specific inhibition of cyclin-dependent kinase 4/6 by PD 0332991 and associated antitumor activity in human tumor xenografts. Mol Cancer Ther. 2004 Nov;3(11):1427-38.

[2]. Goel S, et al. CDK4/6 inhibition triggers anti-tumour immunity. Nature. 2017 Aug 24;548(7668):471-475.

[3]. Richard S Finn, et al. PD 0332991, a selective cyclin D kinase 4/6 inhibitor, preferentially inhibits proliferation of luminal estrogen receptor-positive human breast cancer cell lines in vitro. Breast Cancer Res. 2009;11(5):R77.

[4]. Bollard J, et al. Palbociclib (PD-0332991), a selective CDK4/6 inhibitor, restricts tumour growth in preclinical models of hepatocellular carcinoma. Gut. 2017 Jul;66(7):1286-1296.

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