Palbociclib orotate

Cat. No.: HY-50767D

CAS No.: 2757498-64-7

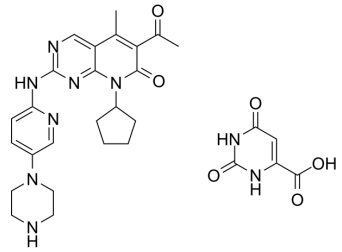
Molecular Formula: $C_{29}H_{33}N_9O_6$

Molecular Weight: 603.63

Target: CDK

Pathway: Cell Cycle/DNA Damage

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

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

IC_{50} & Target

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

In Vitro

Palbociclib (0-1 μM, 24 h) orotate inhibits retinoblastoma 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 (0-10 μM, 24 h) orotate arrests MDA-MB-453 cells exclusively in G1 phase[1].

Palbociclib (500 nM, 7 days) orotate increases expression of homologous genes (H2d1, H2k1, and B2m) in MDA-MB-453 and MDA-MB-361 cells[2].

Palbociclib (0-1 μM, 6 days) orotate 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 (0-1 μM, 3 days) orotate 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 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:	0-1 μM
Incubation Time:	6 days
Result:	Inhibited growth of luminal ER-positive as well as HER2-amplified breast cancer cell lines.

Cell Cycle Analysissup>[1]

Cell Line:	MDA-MB-453 cells

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

In Vivo

Palbociclib (oral adminstration, 75 or 150 mg/kg, daily for 14 days) orotate produces rapid tumor regressions and delays tumor growth[1].

Palbociclib (oral adminstration, 90 mg/kg, daily for 12 days) orotate 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 (oral administration, 100 mg/kg, daily for 1 week) orotate 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
Administration:	Oral administration; daily for 14 days
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
Administration:	Oral administration; daily for 12 days
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
Administration:	Oral administration; daily for 1 week
Result:	Decreased the luminescence signal in liver and delayed tumour growth.

CUSTOMER VALIDATION

- 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.
- Nat Methods. 2022 Mar;19(3):331-340.

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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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