

Product Data Sheet

Product Name: Cobimetinib

Cat. No.: GC10033

Chemical Properties

Cas. No. 934660-93-2

Chemical Name [3,4-difluoro-2-(2-fluoro-4-iodoanilino)phenyl]-[3-hydroxy-3-[(2S)-piperidin-2-yl]azetidin-1-yl]methanone

SMILES C1CCNC(C1)C2(CN(C2)C(=O)C3=C(C(=C(C=C3)F)F)NC4=C(C=C(C=C4)I)F)O

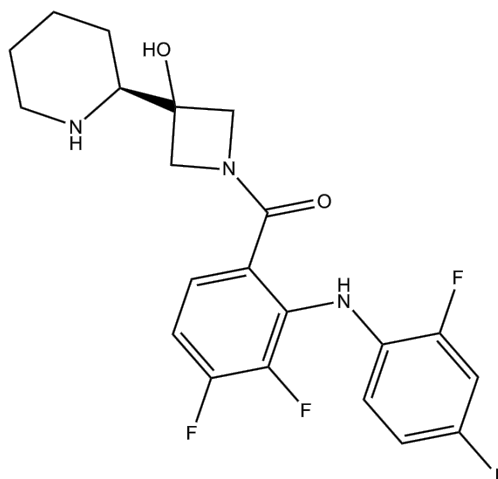
Formula $C_{21}H_{21}F_3IN_3O_2$ M.Wt 531.31

Solubility ≥ 26.55 mg/mL in DMSO, ≥ 33.53 mg/mL in EtOH with gentle warming Storage Store at RT

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Cell lines

RKO cells

RKO cells were cultured in high-glucose Dulbecco modified Eagle medium, with 10% (v/v) of 100U/ml penicillin and 100µg/ml streptomycin added to the medium. Then, cells were placed in a humidified incubator at 37°C and 5% CO₂. After digesting with trypsin, the RKO cells were seeded at a density of 8000 cells per well in a 96-well plate. After overnight incubation, the cells were treated with different concentrations of Cobimetinib (0.05, 0.1, 0.2, 0.4, 0.6, 0.8, and 1.0µM) for 48 hours, with the DMSO (0.1%) treatment group serving as the control group. Then, 10µl of MTT solution (5mg/ml) was added to each well and incubated for 4 hours. After that, 100µl of DMSO was used to replace the supernatant to dissolve the insoluble methylene blue crystals. Finally, the absorbance was measured at 490nm or 570nm.

Reaction
Conditions

0.05, 0.1, 0.2, 0.4, 0.6, 0.8, and 1.0µM; 48h

Applications

Cobimetinib significantly inhibited the viability of RKO cells in a dose-dependent manner.

Animal experiment [2]:

Animal models

SCID mice

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Preparation Method 5×10^7 Hep3B-r cells were injected subcutaneously into the lateral flank of 6-week-old SCID mice at a volume of 100 μ l PBS. When the tumor volume reached approximately 200mm³ (n=5), the mice were orally gavaged with 1mg/kg/day of Cobimetinib. The body weight and tumor size of the mice were monitored twice a day. The tumor length and width were measured with a caliper, and the volume was calculated using the formula: length $\times$ width² $\times$ 0.5236. After 21 days of Cobimetinib treatment, the mice were euthanized and the tumors were isolated for analysis.

Dosage form 1mg/kg/day for 21 days; p.o.

Applications Cobimetinib treatment delayed Hep3B-r tumor growth and inhibited angiogenesis in mice.

References:

- [1] Gong S, Xu D, Zhu J, et al. Efficacy of the MEK inhibitor cobimetinib and its potential application to colorectal cancer cells[J]. Cellular Physiology and Biochemistry, 2018, 47(2): 680-693.
- [2] Tong X, Wang Q, Wu D, et al. MEK inhibition by cobimetinib suppresses hepatocellular carcinoma and angiogenesis in vitro and in vivo[J]. Biochemical and Biophysical Research Communications, 2020, 523(1): 147-152.

Background

Cobimetinib is a potent and selective inhibitor of MEK1 with an IC₅₀ value of 0.9nM^[1]. Cobimetinib can induce a decrease in the activity of phosphorylated ERK, leading to endoplasmic reticulum stress response and promoting cell death^[2]. Cobimetinib has been widely used in xenograft tumor models to inhibit tumor growth^[3].

In vitro, Cobimetinib treatment for 96 hours significantly inhibited the viability of LS174T, RW7213 and RW2982 cells, with IC₅₀ values of 0.28 μ M, 0.23 μ M and 0.44 μ M respectively^[4]. Treatment of HCT116 cells with 1 μ M Cobimetinib for 24 hours led to a decrease in the expression levels of cyclin

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

D1 and cyclin E, an increase in the expression level of p21, and induced G1 phase arrest^[5]. Treatment of IMR-32 cells with 1 μ M Cobimetinib for 24 hours induced PARP cleavage and cell apoptosis^[6].

In vivo, Cobimetinib treatment via oral administration at a dose of 1mg/kg/day for 21 consecutive days significantly inhibited tumor growth, tumor angiogenesis, and ERK signal transduction in the xenograft mouse model of hepatocellular carcinoma^[7]. The combined use of Cobimetinib (10mg/kg/day; p.o.) and venetoclax (100mg/kg/day; p.o.) for 28 consecutive days can reduce the leukemia burden in the mouse model of acute myeloid leukemia and prolong the survival time of the mice^[8].

References:

- [1] Rice K D, Aay N, Anand N K, et al. Novel carboxamide-based allosteric MEK inhibitors: discovery and optimization efforts toward XL518 (GDC-0973)[J]. ACS medicinal chemistry letters, 2012, 3(5): 416-421.
- [2] Corazao-Rozas P, Guerreschi P, André F, et al. Mitochondrial oxidative phosphorylation controls cancer cell's life and death decisions upon exposure to MAPK inhibitors[J]. Oncotarget, 2016, 7(26): 39473.
- [3] Choo E F, Ng C M, Berry L, et al. PK-PD modeling of combination efficacy effect from administration of the MEK inhibitor GDC-0973 and PI3K inhibitor GDC-0941 in A2058 xenografts[J]. Cancer chemotherapy and pharmacology, 2013, 71(1): 133-143.
- [4] Kuracha M R, Thomas P, Loggie B W, et al. Bilateral blockade of MEK-and PI3K-mediated pathways downstream of mutant KRAS as a treatment approach for peritoneal mucinous malignancies[J]. PLoS One, 2017, 12(6): e0179510.
- [5] Gong S, Xu D, Zhu J, et al. Efficacy of the MEK inhibitor cobimetinib and its potential application to colorectal cancer cells[J]. Cellular Physiology and Biochemistry, 2018, 47(2): 680-693.
- [6] Singh A, Ruan Y, Tippet T, et al. Targeted inhibition of MEK1 by cobimetinib leads to differentiation and apoptosis in neuroblastoma cells[J]. Journal of Experimental & Clinical Cancer Research, 2015, 34(1): 104.
- [7] Tong X, Wang Q, Wu D, et al. MEK inhibition by cobimetinib suppresses hepatocellular carcinoma and angiogenesis in vitro and in vivo[J]. Biochemical and Biophysical Research Communications, 2020, 523(1): 147-152.
- [8] Han L, Zhang Q, Dail M, et al. Concomitant targeting of BCL2 with venetoclax and MAPK signaling with cobimetinib in acute myeloid leukemia models[J]. Haematologica, 2019, 105(3): 697.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA