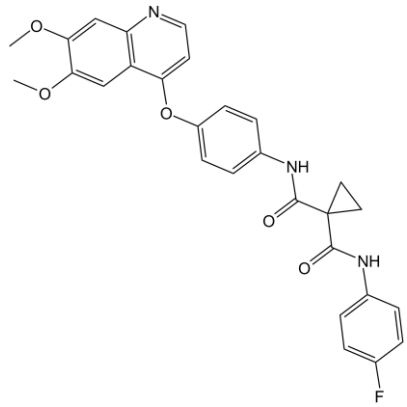
Product Data Sheet

Chemical Properties

Product Name: Cabozantinib (XL184, BMS-907351)



Cas No.: 849217-68-1

M.Wt: 501.51

Formula: C28H24FN3O5

Chemical Name: 1-N-[4-(6,7-dimethoxyquinolin-4-yl)oxyphenyl]-1-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide

Canonical SMILES: COC1=CC2=C(C=CN=C2C=C1OC)OC3=CC=C(C=C3)NC(=O)C4(CC4)C(=O)NC5=CC=C(C=C5)F

Solubility: ≥25.1mg/mL in DMSO

Storage: Store at -20°C

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.

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

Biological Activity

Targets : Tyrosine Kinase

Pathways: c-MET

Description:

Cabozantinib (also called XL184, BMS-907351 Cometriq [1]), is an inhibitor of multiple receptor tyrosine kinases (RTKs), including vascular endothelial growth factor receptor 2 (VEGFR2), hepatocyte growth factor receptor (MET), and rearranged during transfection (RET) [2] [3], with IC50 values of 0.035 nmol/L, 1.3 nmol/L and 5.2 nmol/L to VEGFR2, MET and RET, respectively

[4].
RTKs transmit a wide array of extracellular signals for regulating differentiation and proliferation to cells. Ligand binding triggers many events such as autophosphorylation of tyrosine residues and receptor dimerization [5].
TT cell line was a human MTC cell line that had an activating C634W RET mutant and was expressing calcitonin. In this cell line, cabozantinib inhibited the autophosphorylation of RET with an IC50 value of 85 nmol/L. In TT cells grown for 72 h in 10% serum, cabozantinib dose-dependently inhibited cell proliferation with an IC50 value of 94 nmol/L [4].
Administrated with cabozantinib daily orally at doses of 10, 30, or 60 mg/kg, nu/nu mice bearing TT xenograft tumors, showed a significantly inhibited tumor growth compared with vehicle-treated group. At both doses of 30 and 60 mg/kg, cabozantinib caused markedly and significantly reduced circulating calcitonin (75%; $p < 0.005$) in serum compared with vehicle-treated control animals [4].

***Reference**:*

[1]. Michael G. Doran, Daniel E. Spratt, John Wongvipat, et al. Cabozantinib Resolves Bone Scans in Tumor-Naïve Mice Harboring Skeletal Injuries. Molecular Imaging, 2014, 13:1-5.
[2]. Rossella Elisei, Martin J. Schlumberger, Stefan P. Müller, et al. Cabozantinib in Progressive Medullary Thyroid Cancer. J. Clin. Oncol., 2013, 31(29):3639-46.
[3]. Razelle Kurzrock, Steven I. Sherman, Douglas W. Ball, et al. Activity of XL184 (Cabozantinib), an Oral Tyrosine Kinase Inhibitor, in Patients with Medullary Thyroid Cancer. J. Clin. Oncol., 2011, 29(19):2660-6.
[4]. Frauke Bentzien, Marcus Zuzow, Nathan Heald, et al. In Vitro and In Vivo Activity of Cabozantinib (XL184), an Inhibitor of RET, MET, and VEGFR2, in a Model of Medullary Thyroid Cancer. Thyroid, 2013, 23(12):1569-1577.
[5]. Xianhua Piao, Robert Paulson, Peter van der Geer, et al. Oncogenic mutation in the Kit receptor tyrosine kinase alters substrate specificity and induces degradation of the protein tyrosine phosphatase SHP-1. Proc. Natl. Acad. Sci. USA., 1996, 93(25):14665-14669.

Protocol

Cell experiment:

Cell lines	Human microvascular endothelial (HMVEC) 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	IC50: 6.7 nM, 7 days
Applications	HMVEC cells were incubated with VEGF in the presence of cabozantinib and tubule formation visualized by immunostaining for CD31. Cabozantinib inhibited tubule formation with an IC50 value of 6.7 nM with no evidence of cytotoxicity, showing that cabozantinib exerts an antiangiogenic rather than cytotoxic effect.

Animal experiment [3]:

Animal models	Female nu/nu mice implanted with H441 cells
Dosage form	Oral administration, 100 mg/kg, 8 hours
Applications	A single 100 mg/kg oral dose of cabozantinib resulted in inhibition of phosphorylation of MET 2 to 8 hours postdose in H441 tumors that harbor constitutively phosphorylated MET. This effect was reversible, as MET phosphorylation returned to basal levels by 48 hours after treatment.
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.

***Reference**:*
[1] Yakes F M, Chen J, Tan J, et al. Cabozantinib (XL184), a novel MET and VEGFR2 inhibitor, simultaneously suppresses metastasis, angiogenesis, and tumor growth. Molecular cancer therapeutics, 2011, 10(12): 2298-2308.

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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