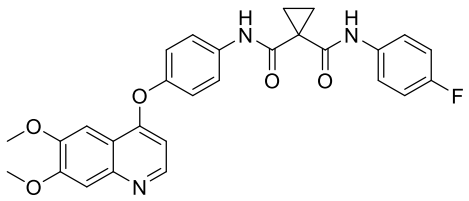
Product data sheet

MedKoo Cat#: 200595 Name: Cabozantinib (free base) CAS#: 849217-68-1 (free base) Chemical Formula: $C_{28}H_{24}FN_3O_5$ Exact Mass: 501.17 Molecular Weight: 501.51	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

Cabozantinib, also known as XL-184 or BMS-907351, is an orally bioavailable, small molecule receptor tyrosine kinase (RTK) inhibitor with potential antineoplastic activity. Cabozantinib strongly binds to and inhibits several tyrosine receptor kinases. Specifically, cabozantinib appears to have a strong affinity for the hepatocyte growth factor receptor (Met) and vascular endothelial growth factor receptor 2 (VEGFR2), which may result in inhibition of tumor growth and angiogenesis, and tumor regression. Cabozantinib was approved by the U.S. FDA in November 2012 for the treatment of medullary thyroid cancer.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	46.29	92.30
DMSO:PBS (pH 7.2) (1:2)	0.3	0.60
DMF	3.0	5.98
Ethanol	2.0	3.99

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	1.99 mL	9.97 mL	19.94 mL
5 mM	0.40 mL	1.99 mL	3.99 mL
10 mM	0.20 mL	1.00 mL	1.99 mL
50 mM	0.04 mL	0.20 mL	0.40 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Lei ZN, Teng QX, Gupta P, Zhang W, Narayanan S, Yang DH, Wurpel JND, Fan YF, Chen ZS. Cabozantinib Reverses Topotecan Resistance in Human Non-Small Cell Lung Cancer NCI-H460/TPT10 Cell Line and Tumor Xenograft Model. Front Cell Dev Biol. 2021 Mar 22;9:640957. doi: 10.3389/fcell.2021.640957. PMID: 33829017; PMCID: PMC8019832.
2. Pan T, Martinez M, Hubka KM, Song JH, Lin SC, Yu G, Lee YC, Gallick GE, Tu SM, Harrington DA, Farach-Carson MC, Lin SH, Satcher RL. Cabozantinib Reverses Renal Cell Carcinoma-mediated Osteoblast Inhibition in Three-dimensional Coculture In Vitro and Reduces Bone Osteolysis In Vivo. Mol Cancer Ther. 2020 Jun;19(6):1266-1278. doi: 10.1158/1535-7163.MCT-19-0174. Epub 2020 Mar 27. PMID: 32220969; PMCID: PMC7272308.

In vivo study

Product data sheet

1. Labrecque MP, Brown LG, Coleman IM, Nguyen HM, Lin DW, Corey E, Nelson PS, Morrissey C. Cabozantinib can block growth of neuroendocrine prostate cancer patient-derived xenografts by disrupting tumor vasculature. PLoS One. 2021 Jan 20;16(1):e0245602. doi: 10.1371/journal.pone.0245602. PMID: 33471819; PMCID: PMC7817027.
2. Zhang X, Zhu M, Xie L, Sun X, Xu J, Guo Y, Liu D, Shi Y, Xu X, Song E. Cabozantinib, a Multityrosine Kinase Inhibitor of MET and VEGF Receptors Which Suppresses Mouse Laser-Induced Choroidal Neovascularization. J Ophthalmol. 2020 Jun 19;2020:5905269. doi: 10.1155/2020/5905269. PMID: 32655941; PMCID: PMC7322600.

7. Bioactivity

Biological target:

Cabozantinib is a multiple receptor tyrosine kinases (RTKs) inhibitor that inhibits VEGFR2, c-Met, Kit, Axl and Flt3 with IC50s of 0.035, 1.3, 4.6, 7 and 11.3 nM, respectively.

In vitro activity

As shown in Figure 1B, CBZ (Cabozantinib), at a non-toxic concentration (5 μM), could significantly decrease the IC50 value of TPT in NCI-H460/TPT10 cells. The cross-resistance to other ABCG2 substrates in NCI-H460/TPT10 cells, including mitoxantrone and SN-38, could also be reversed by CBZ with comparable potency to the ABCG2 inhibitor Ko143 (Table 1). On the other hand, the IC50 value of cisplatin, which is not a substrate of ABCG2, was not affected by co-administration of 5 μM CBZ (Figure 1C). Furthermore, CBZ could restore TPT accumulation in ABCG2 overexpressing NCI-H460/TPT10 cells (Figures 1D,E). These observations indicated that the CBZ can alleviate TPT resistance most likely by increasing intracellular TPT level, which could be a result from the ABCG2 inhibitory effect of CBZ. A slight reduction of TPT IC50 and elevation of TPT accumulation in parental NCI-H460 cells treated with CBZ were observed (Figures 1B,D,E), possibly due to the endogenous ABCG2 expression in NCI-H460 cells.

Reference: Front Cell Dev Biol. 2021; 9: 640957. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8019832/

In vivo activity

To further confirm the role of CBZ (Cabozantinib) in the alleviation of CNV (choroidal neovascularization), CBZ oral gavage at the dose of 200 or 300 mg/kg/day was performed on the same day of laser injury and analysis was performed at 14 d (Figure 5(a)). FFA showed decreased CNV leakage in the CBZ groups (Figure 5(b), a, b, and c). Leakage score analysis also showed that the grade percentage of score 0 and score 1 increased, while the grade percentage of score 2b was decreased in the CBZ groups (Figure 5(c)). IB4 and phalloidin double staining indicated that the CNV lesion area was decreased in the CBZ groups (Figure 5(b) (d-3, e-3, f-3) and 5(d)). Additionally, CBZ oral gavage downregulated the HGF, p-MET, and p-VEGFR2 protein levels in CNV in the 14 d groups (Figures 5(e) and 5(f)). Furthermore, CBZ showed no effect on vascular leakage and formation in the normal mice (Figure 5(b)). The results suggest that CBZ oral gavage mitigates CNV leakage and the CNV lesion area via restraining the phosphorylation of MET and VEGFR2.

Reference: J Ophthalmol. 2020; 2020: 5905269. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7322600/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.