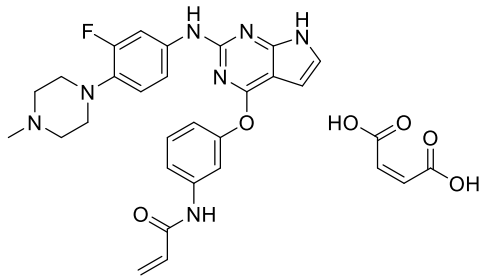
Product data sheet

MedKoo Cat#: 206774 Name: Abivertinib maleate CAS#: 1557268-88-8 (maleate) Chemical Formula: $C_{30}H_{30}FN_7O_6$ Molecular Weight: 603.6114	
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:

Abivertinib, also known as avitinib, AC0010 or AC0010MA, is an orally available, irreversible, epidermal growth factor receptor (EGFR) mutant-selective inhibitor, with potential antineoplastic activity. Upon oral administration, avitinib covalently binds to and inhibits the activity of mutant forms of EGFR, including the drug-resistant T790M EGFR mutant, which prevents signaling mediated by mutant forms of EGFR. This may both induce cell death and inhibit tumor growth in EGFR-mutated tumor cells. EGFR, a receptor tyrosine kinase that is mutated in a variety of cancers, plays a key role in tumor cell proliferation and tumor vascularization. As this agent is selective towards mutant forms of EGFR, its toxicity profile may be reduced when compared to non-selective EGFR inhibitors, which also inhibit wild-type EGFR.

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	100.0	165.67

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.66 mL	8.28 mL	16.57 mL
5 mM	0.33 mL	1.66 mL	3.31 mL
10 mM	0.17 mL	0.83 mL	1.66 mL
50 mM	0.03 mL	0.17 mL	0.33 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. Huang S, Yu M, Shi N, Zhou Y, Li F, Li X, Huang X, Jin J. Apigenin and Abivertinib, a novel BTK inhibitor synergize to inhibit diffuse large B-cell lymphoma in vivo and vitro. J Cancer. 2020 Feb 3;11(8):2123-2132. doi: 10.7150/jca.34981. PMID: 32127939; PMCID: PMC7052937.

2. Huang S, Li C, Zhang X, Pan J, Li F, Lv Y, Huang J, Ling Q, Ye W, Mao S, Huang X, Jin J. Abivertinib synergistically strengthens the anti-leukemia activity of venetoclax in acute myeloid leukemia in a BTK-dependent manner. Mol Oncol. 2020 Oct;14(10):2560-2573. doi: 10.1002/1878-0261.12742. Epub 2020 Jul 3. PMID: 32519423; PMCID: PMC7530784.

In vivo study

1. Huang S, Yu M, Shi N, Zhou Y, Li F, Li X, Huang X, Jin J. Apigenin and Abivertinib, a novel BTK inhibitor synergize to inhibit diffuse large B-cell lymphoma in vivo and vitro. J Cancer. 2020 Feb 3;11(8):2123-2132. doi: 10.7150/jca.34981. PMID: 32127939; PMCID: PMC7052937.

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2. Huang S, Li C, Zhang X, Pan J, Li F, Lv Y, Huang J, Ling Q, Ye W, Mao S, Huang X, Jin J. Abivertinib synergistically strengthens the anti-leukemia activity of venetoclax in acute myeloid leukemia in a BTK-dependent manner. Mol Oncol. 2020 Oct;14(10):2560-2573. doi: 10.1002/1878-0261.12742. Epub 2020 Jul 3. PMID: 32519423; PMCID: PMC7530784.

7. Bioactivity

Biological target:

Avitinib maleate is a pyrrolopyrimidine-based irreversible epidermal growth factor receptor (EGFR) inhibitor with an IC50 of 7.68 nM.

In vitro activity

A proliferation assay with an appropriate concentration of Apigenin in combination with low-dose Abivertinib was examined in U2932 and OCI-LY10 for 48 hours. The results indicate that the cell viability of the combined group is significantly lower than either of the single drug groups (Fig. 3A, B). Next, the results of soft agar colony formation experiments further confirmed that the colony forming ability of the combined group in U2932 is sufficiently inhibited (Fig. 3D). In order to further explore the mechanism of the combination effect, apoptosis was detected in combination and single treatment groups. The results are shown in Fig. 3E and and 3F: the combination of two drugs at a lower concentration can significantly induce apoptosis and is more than any single drug group. In the search for apoptotic mechanisms, it was concluded that the combination of two drugs can down-regulate the anti-apoptotic proteins of BCL2 and BCL-XL (Fig. 4A), while the cleaved-PARP, cleaved-C3, cleaved-C8 were also captured (Fig. 4B). Meanwhile, the expression level of BCL-2 and BCL-XL of different treatment groups was studied by Westernblot assay of tumor tissue moved from DLBCL xenograft and turned out the similar result to cell lines (Fig. 4D). According to the results, it was concluded that Apigenin synergizes with Abivertinib to induce apoptosis in diffuse large B-cell lymphoma by down-regulating BCL2, BCL-XL and activating the caspase family.

Reference: J Cancer. 2020 Feb 3;11(8):2123-2132. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/32127939/

In vivo activity

All mice were treated as described in methods. Representative tumors in the xenograft mice treated in different groups are shown in Fig. 5A, the treatments of Apigenin and Abivertinib or their combination significantly reduced tumor mass compared to vehicle. In details, Apigenin, Abivertinib, COM decreased by 32.5%, 48%, 80% the tumor weight compared to vehicle group respectively (Fig. 5B).The similar results were found when refer to tumor size(Fig. 5C). Next, the tumor progression was analyzed by measuring the size of tumors in each group every 2 days, the result shown in Fig. 5D, the treatments effectively inhibit the growing of tumors. In order to measure the apoptosis induced by drugs, tunnel assay was played, the results showed increase in combination group (Fig. 5E and F). When the tumor burden on spleen and liver of mice was analyzed, the HE staining showed no significant difference among groups on liver while decreasing extramedullary hematopoiesis in combination group (Fig. 5G). All the results unveiled the fact that Apigenin can inhibit the DLBCL progression and can cooperate with Abivertinib to achieve better anti-lymphoma function.

Reference: J Cancer. 2020 Feb 3;11(8):2123-2132. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/32127939/