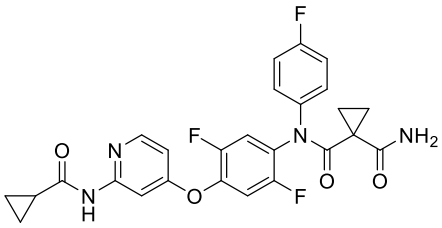
Product data sheet

MedKoo Cat#: 206143 Name: Altiratinib CAS#: 1345847-93-9 Chemical Formula: $C_{26}H_{21}F_3N_4O_4$ Exact Mass: 510.15149 Molecular Weight: 510.46	
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:
Altiratinib, also known as DCC-270, DP-5164, is an oral, selective and highly potent inhibitor of MET, TIE2, VEGFR2 and TRK kinases with potential anticancer activity. DCC-2701 effectively reduces tumor burden in vivo and blocks c-MET pTyr(1349)-mediated signaling, cell growth and migration as compared with a HGF antagonist in vitro. Importantly, DCC-2701's anti-proliferative activity was dependent on c-MET activation induced by stromal human fibroblasts and to a lesser extent exogenous HGF.

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	45.0	88.16
DMSO:PBS (pH 7.2) (1:2)	0.33	0.65
DMF	10.0	19.59

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.96 mL	9.80 mL	19.59 mL
5 mM	0.39 mL	1.96 mL	3.92 mL
10 mM	0.20 mL	0.98 mL	1.96 mL
50 mM	0.04 mL	0.20 mL	0.39 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. Somwar R, Hofmann NE, Smith B, Odintsov I, Vojnic M, Linkov I, Tam A, Khodos I, Mattar MS, de Stanchina E, Flynn D, Ladanyi M, Drilon A, Shinde U, Davare MA. NTRK kinase domain mutations in cancer variably impact sensitivity to type I and type II inhibitors. Commun Biol. 2020 Dec 16;3(1):776. doi: 10.1038/s42003-020-01508-w. PMID: 33328556; PMCID: PMC7745027.
2. Kwon Y, Smith BD, Zhou Y, Kaufman MD, Godwin AK. Effective inhibition of c-MET-mediated signaling, growth and migration of ovarian cancer cells is influenced by the ovarian tissue microenvironment. Oncogene. 2015 Jan 8;34(2):144-53. doi: 10.1038/onc.2013.539. Epub 2013 Dec 23. PMID: 24362531; PMCID: PMC4067476.

In vivo study

1. Piao Y, Park SY, Henry V, Smith BD, Tiao N, Flynn DL, de Groot JF. Novel MET/TIE2/VEGFR2 inhibitor altiratinib inhibits tumor growth and invasiveness in bevacizumab-resistant glioblastoma mouse models. Neuro Oncol. 2016 Sep;18(9):1230-41. doi: 10.1093/neuonc/now030. Epub 2016 Mar 9. PMID: 26965451; PMCID: PMC4998992.

2. Smith BD, Kaufman MD, Leary CB, Turner BA, Wise SC, Ahn YM, Booth RJ, Caldwell TM, Ensinger CL, Hood MM, Lu WP, Patt TW, Patt WC, Rutkoski TJ, Samarakoon T, Telikepalli H, Vogeti L, Vogeti S, Yates KM, Chun L, Stewart LJ, Clare M, Flynn DL. Altiratinib Inhibits Tumor Growth, Invasion, Angiogenesis, and Microenvironment-Mediated Drug Resistance via Balanced Inhibition of MET, TIE2, and VEGFR2. Mol Cancer Ther. 2015 Sep;14(9):2023-34. doi: 10.1158/1535-7163.MCT-14-1105. Epub 2015 Aug 18. PMID: 26285778.

7. Bioactivity

Biological target:

Altiratinib (DCC-2701) is a multi-targeted kinase inhibitor with IC50s of 2.7, 8, 9.2, 9.3, 0.85, 4.6, 0.83 nM for MET, TIE2, VEGFR2, FLT3, Trk1, Trk2, and Trk3 respectively.

In vitro activity

Here this study tested if the type II inhibitor altiratinib would suppress the growth of Ba/F3 TPM3-NTRK1G595R and ETV6-NTRK3G623R cells using viability assays. These data show that NTRK1G595R is resistant to both larotrectinib and altiratinib (Fig. 2a, b). However, NTRK3G623R retains partial sensitivity to altiratinib (IC50 ~ 240 nM) as compared to near-total resistance to larotrectinib (IC50 > 2000 nM). This study performed immunoblotting to assess on-target NTRK inhibition from treated Ba/F3 cell lysates. These data suggest that altiratinib may indeed retain some inhibitory propensity against NTRK3G623R as compared to NTRK1G595R (Fig. 2c, d). Densitometry reveals that NTRKG623R autophosphorylation is ~95% attenuated with 250 nM altiratinib (Fig. 2d, Supplementary Fig. 3b) whereas 250 nM larotrectinib inhibited NTRKG623R by only ~41% (Fig. 2d, Supplementary Fig. 3a).

Reference: Commun Biol. 2020; 3: 776. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7745027/

In vivo activity

Altiratinib was evaluated in the MET-amplified MKN-45 xenograft mouse model to determine the pharmacokinetic/pharmacodynamic relationship for in vivo MET target inhibition. A single oral dose of 30 mg/kg altiratinib led to >95% inhibition of MET phosphorylation for the entire 24-hour period (Supplementary Table S4A). A single 10 mg/kg oral dose of altiratinib (Fig. 2D; Supplementary Table S4B) exhibited complete inhibition of MET phosphorylation through 12 hours and 73% inhibition at 24 hours postdose [factoring in plasma protein binding (98.7% bound)], the free drug concentrations required for MET inhibition correlated with in vitro results (IC50 $\approx$ 1.1 ng/mL = 2.2 nmol/L; Table 2).

Reference: Mol Cancer Ther. 2015 Sep;14(9):2023-34. https://mct.aacrjournals.org/content/14/9/2023.long

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.