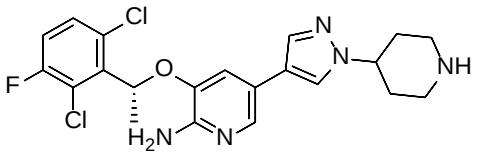
Product data sheet

MedKoo Cat#: 202222 Name: Crizotinib CAS#: 877399-52-5 (free base) Chemical Formula: $C_{21}H_{22}Cl_2FN_5O$ Exact Mass: 449.1185 Molecular Weight: 450.34	
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:
Crizotinib, also known as PF-02341066, is an orally bioavailable agent belonging to the class of c-met/hepatocyte growth factor receptor (HGFR) tyrosine kinase inhibitors with potential antineoplastic activity. Crizotinib was approved for treatment of some non-small cell lung carcinoma (NSCLC) in the US, and undergoing clinical trials testing its safety and efficacy in anaplastic large cell lymphoma, neuroblastoma, and other advanced solid tumors in both adults and childre. Crizotinib inhibits the membrane receptor MET and activation of the MET signaling pathway, which may block tumor cell growth, migration and invasion, and tumor angiogenesis in susceptible tumor cell populations. Crizotinib was approved in 2011.

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	10.13	22.49
DMF	5.0	11.10
DMF:PBS (pH 7.2) (1:1)	0.50	1.11
Ethanol	0.50	1.11

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.22 mL	11.10 mL	22.21 mL
5 mM	0.44 mL	2.22 mL	4.44 mL
10 mM	0.22 mL	1.11 mL	2.22 mL
50 mM	0.04 mL	0.22 mL	0.44 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. Kim KS, Jiang C, Kim JY, Park JH, Kim HR, Lee SH, Kim HS, Yoon S. Low-Dose Crizotinib, a Tyrosine Kinase Inhibitor, Highly and Specifically Sensitizes P-Glycoprotein-Overexpressing Chemoresistant Cancer Cells Through Induction of Late Apoptosis in vivo and in vitro. Front Oncol. 2020 May 12;10:696. doi: 10.3389/fonc.2020.00696. PMID: 32528877; PMCID: PMC7247847.

In vivo study

1. Kim KS, Jiang C, Kim JY, Park JH, Kim HR, Lee SH, Kim HS, Yoon S. Low-Dose Crizotinib, a Tyrosine Kinase Inhibitor, Highly and Specifically Sensitizes P-Glycoprotein-Overexpressing Chemoresistant Cancer Cells Through Induction of Late Apoptosis in vivo and in vitro. Front Oncol. 2020 May 12;10:696. doi: 10.3389/fonc.2020.00696. PMID: 32528877; PMCID: PMC7247847.

7. Bioactivity

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Biological target: Crizotinib (PF-02341066) is an ALK and c-Met inhibitor with IC50s of 20 and 8 nM, respectively.

In vitro activity

Whether crizotinib induces apoptotic cell death was tested using annexin V analysis. As seen in Figure 2D, apoptotic cell death was greatly increased after treatment with 5 μM crizotinib, compared to treatment with the control. This indicated that the reduction in the number of cells at the G2 arrest stage by crizotinib contributes to increased apoptotic death. In a detailed analysis of annexin V, it was determined whether early or late apoptotic cellular death was increased when the drug concentration increased. As seen in Figures 2D,E, crizotinib at 10 μM largely increased late apoptosis in comparison with 5 μM crizotinib, whereas early apoptosis was not increased much. This suggests that crizotinib could directly induce apoptotic cellular death, without delay, via the early apoptotic pathway. Overall, low-dose crizotinib strongly sensitized P-gp-overexpressing resistant KBV20C cells via G2 cell cycle arrest and apoptosis.

Reference: Front Oncol. 2020 May 12;10:696. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7247847/

In vivo activity

The antitumor action of crizotinib was examined in in vivo BALB/c nude mouse xenograft models of drug-resistant KBV20C cells and drug-sensitive parent KB cells. As shown in Figures 4A–C, treatment of nude mice with crizotinib markedly inhibited the resistant KBV20C tumor growth compared with vehicle treatment. Detailed analysis showed that crizotinib treatment significantly reduced the tumor volume by 50% (Figure 4A) and tumor weight by ~40% (Figures 4B,C), relative to the control group. These data show that crizotinib significantly inhibited the growth of KBV20C cells in vivo. Furthermore, whether crizotinib showed a lower sensitizing-effect on drug-sensitive parent KB cells in the in vivo xenograft model (Figures 2D,E, 3B) was tested. As expected, drug-sensitive KB cells showed a VIC treatment time-dependent inhibition of tumor growth compared with the control group, whereas drug-resistant KBV20C cells were not affected by VIC treatment (Figures 4A,D). It was confirmed that crizotinib had a greater effect on KBV20C cells than on KB cells in the in vivo xenograft model (Figures 4A–F). This suggests that crizotinib specifically sensitizes drug-resistant cancer cells.

Reference: Front Oncol. 2020 May 12;10:696. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7247847/