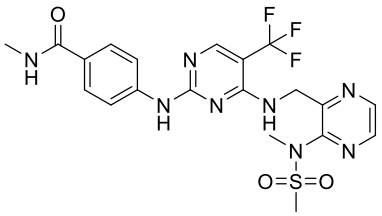
Product data sheet

MedKoo Cat#: 205583 Name: Defactinib free base CAS#: 1073154-85-4 (free base) Chemical Formula: $C_{20}H_{21}F_3N_8O_3S$ Exact Mass: 510.14094 Molecular Weight: 510.49	
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:

Defactinib, also known as VS-6063 and PF-04554878, is an orally bioavailable, small-molecule focal adhesion kinase (FAK) inhibitor with potential antiangiogenic and antineoplastic activities. FAK inhibitor PF-04554878 inhibits FAK, which may prevent the integrin-mediated activation of several downstream signal transduction pathways, including ERK, JNK/MAPK and PI3K/Akt, thus inhibiting tumor cell migration, proliferation and survival.

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	18.67	36.57
DMSO:PBS (pH 7.2) (1:3)	0.25	0.49
DMF	1.0	1.96

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.96 mL	9.79 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. Fu Y, Zhang Y, Lei Z, Liu T, Cai T, Wang A, Du W, Zeng Y, Zhu J, Liu Z, Huang JA. Abnormally activated OPN/integrin αVβ3/FAK signalling is responsible for EGFR-TKI resistance in EGFR mutant non-small-cell lung cancer. J Hematol Oncol. 2020 Dec 7;13(1):169. doi: 10.1186/s13045-020-01009-7. PMID: 33287873; PMCID: PMC7720454.
2. Zhang L, Zhao D, Wang Y, Zhang W, Zhang J, Fan J, Zhan Q, Chen J. Focal adhesion kinase (FAK) inhibitor-defactinib suppresses the malignant progression of human esophageal squamous cell carcinoma (ESCC) cells via effective blockade of PI3K/AKT axis and downstream molecular network. Mol Carcinog. 2021 Feb;60(2):113-124. doi: 10.1002/mc.23273. Epub 2020 Dec 6. PMID: 33283357.

In vivo study

1. Hu Y, Wu H, Xu T, Wang Y, Qin H, Yao Z, Chen P, Xie Y, Ji Z, Yang K, Chai Y, Zhang X, Yu B, Cui Z. Defactinib attenuates osteoarthritis by inhibiting positive feedback loop between H-type vessels and MSCs in subchondral bone. J Orthop Translat. 2020 May 19;24:12-22. doi: 10.1016/j.jot.2020.04.008. PMID: 32518750; PMCID: PMC7261948.

2. Kolev VN, Tam WF, Wright QG, McDermott SP, Vidal CM, Shapiro IM, Xu Q, Wicha MS, Pachter JA, Weaver DT. Inhibition of FAK kinase activity preferentially targets cancer stem cells. Oncotarget. 2017 Jun 16;8(31):51733-51747. doi: 10.18632/oncotarget.18517. PMID: 28881682; PMCID: PMC5584283.

7. Bioactivity

Biological target:

Defactinib (VS-6063; PF-04554878) is a FAK inhibitor.

In vitro activity

As shown in Figure 1A, defactinib treatment for 72 h dose-dependently decreased the viability of these indicated ESCC cell lines (Figure 1A). This study further observed the anti-invasive or migratory ability of defactinib in KYSE410 and KYSE510 using Transwell assay. As shown in Figure 1B,C, defactinib dose-dependently inhibited the migration and invasion of indicated ESCC cells. Taken together, these results indicate that defactinib exerts excellent antitumor effects in ESCC cells.

Reference: Mol Carcinog. 2021 Feb;60(2):113-124. https://pubmed.ncbi.nlm.nih.gov/33283357/

In vivo activity

In this study, FAK expression was elevated significantly in the subchondral bone of the vehicle-treated ACLT mice in comparison with the sham controls and defactinib (FAK inhibitor)-treated ACLT mice (Fig. 1A). Through CT-based microangiography, the vessel number (VN) and vessel volume/total tissue volume (VV/TV) increased significantly in the subchondral bone of the vehicle-treated ACLT mice (Fig. 1B–D), whereas defactinib treatment normalized them. These demonstrated that the vasculature in the subchondral bone was significantly elevated during the onset of OA. The increase in the vasculature was from H-type vessels. Double immunofluorescence staining of CD31 and endomucin revealed a significant increase in H-type vessels ($CD31^+$ $endomucin^+$) in the subchondral bone marrow of vehicle-treated ACLT mice, whereas defactinib treatment lowered H-type vessels with no significant difference relative to the sham controls (Fig. 1E and F). Taken together, these results demonstrate that an increase in FAK modulates H-type vessel formation during the onset of OA.

Reference: J Orthop Translat. 2020 Sep; 24: 12–22. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7261948/

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.