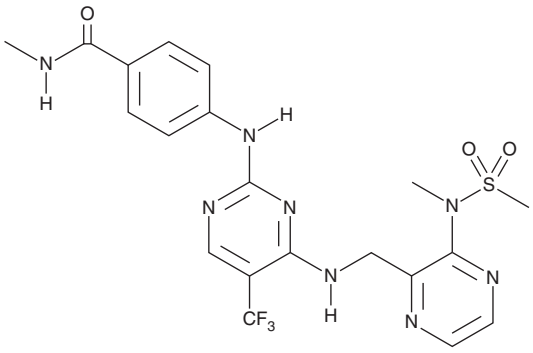
PRODUCT INFORMATION

Defactinib

Item No. 17737

CAS Registry No.:	1073154-85-4
Formal Name:	N-methyl-4-[[4-[[[3-[methyl(methylsulfonyl)amino]-2-pyrazinyl]methyl]amino]-5-(trifluoromethyl)-2-pyrimidinyl]amino]-benzamide
Synonyms:	PF-04554878, VS-6063
MF:	$C_{20}H_{21}F_3N_8O_3S$
FW:	510.5
Purity:	≥98%
UV/Vis.:	λ_{max}: 220, 307 nm
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

Defactinib is supplied as a crystalline solid. A stock solution may be made by dissolving the defactinib in the solvent of choice, which should be purged with an inert gas. Defactinib is soluble in organic solvents such as DMSO and dimethyl formamide. The solubility of defactinib in these solvents is approximately 1 mg/ml.

Defactinib is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, defactinib should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. Defactinib has a solubility of approximately 0.25 mg/ml in a 1:3 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

Focal adhesion kinase (FAK) is a non-receptor tyrosine kinase that plays a vital role in many oncogenic pathways.[1,2] Defactinib is a dose-dependent inhibitor of FAK, with maximal inhibition of FAK autophosphorylation in cells achieved at 10 µM.[3] It is less effective against the related kinase PYK2. Defactinib restores the chemosensitivity of taxane-resistant cells to paclitaxel (Item No. 10461), although it is not cytotoxic alone.[3] Defactinib decreases YB-1 phosphorylation and nuclear accumulation in an Akt-dependent manner. It is orally bioavailable, inhibiting FAK and augmenting paclitaxel action in suppressing the growth and number of ovarian cancer cell tumors in mice.[3]

References

1. Schwock, J., Dhani, N., and Hedley, D.W. Targeting focal adhesion kinase signaling in tumor growth and metastasis. *Expert Opin. Ther. Targets* **14(1)**, 77-94 (2010).
2. Lee, B.Y., Timpson, P., Horvath, L.G., *et al.* FAK signaling in human cancer as a target for therapeutics. *Pharmacol. Ther.* **146**, 132-149 (2015).
3. Kang, Y., Hu, W., Ivan, C., *et al.* Role of focal adhesion kinase in regulating YB-1-mediated paclitaxel resistance in ovarian cancer. *JNCI* **105(19)**, 1485-1495 (2013).

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