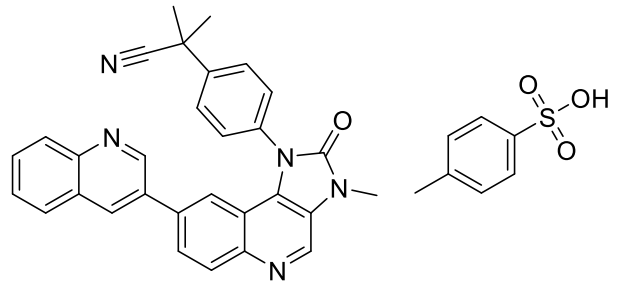
Product data sheet

MedKoo Cat#: 581211 Name: Dactolisib tosylate CAS#: 1028385-32-1 (tosylate) Chemical Formula: $C_{37}H_{31}N_5O_4S$ Exact Mass: 641.2097 Molecular Weight: 641.7	
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:

Dactolisib tosylate is also known as NVP-BEZ 235 Tosylate. NVP-BEZ235 is an imidazo[4,5-c]quinoline derivative that inhibits PI3K and mTOR kinase activity by binding to the ATP-binding cleft of these enzymes. The IC50s for PI3Kα, β, γ, δ are 4, 75, 7, 5 nM, respectively. It is also found to be as active against the mutant PI3KαE545K or PI3KαH1047R with IC50s of 5.7 and 4.6 nM, respectively. In human tumor cell lines, it is able to effectively and specifically block the dysfunctional activation of the PI3K pathway, inducing G1 arrest. PTEN-null cell lines PC3M and U87MG shows a dose-dependent reduction in cell proliferation when treated with increasing concentrations of NVP-BEZ235, with an average GI50 of 10 to 12 nM. In Vivo NVP-BEZ235 is well tolerated, displays disease stasis when administered orally, and enhances the efficacy of other anticancer agents. At a dose of 50 mg/kg, NVP-BEZ235 appears rapidly in plasma with a Cmax of 1.68 μM at 0.5 h and a C24h of 0.03 μM.

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	34.0	52.98

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.56 mL	7.79 mL	15.58 mL
5 mM	0.31 mL	1.56 mL	3.12 mL
10 mM	0.16 mL	0.78 mL	1.56 mL
50 mM	0.03 mL	0.16 mL	0.31 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. Cai J, Xia J, Zou J, Wang Q, Ma Q, Sun R, Liao H, Xu L, Wang D, Guo X. The PI3K/mTOR dual inhibitor NVP-BEZ235 stimulates mutant p53 degradation to exert anti-tumor effects on triple-negative breast cancer cells. FEBS Open Bio. 2020 Apr;10(4):535-545. doi: 10.1002/2211-5463.12806. Epub 2020 Mar 6. PMID: 32027103; PMCID: PMC7137801.
2. Deng L, Jiang L, Lin XH, Tseng KF, Liu Y, Zhang X, Dong RH, Lu ZG, Wang XJ. The PI3K/mTOR dual inhibitor BEZ235 suppresses proliferation and migration and reverses multidrug resistance in acute myeloid leukemia. Acta Pharmacol Sin. 2017 Mar;38(3):382-391. doi: 10.1038/aps.2016.121. Epub 2017 Jan 2. PMID: 28042875; PMCID: PMC5342661.

In vivo study

1. Ruan B, Liu W, Chen P, Cui R, Li Y, Ji M, Hou P, Yang Q. NVP-BEZ235 inhibits thyroid cancer growth by p53-dependent/independent p21 upregulation. Int J Biol Sci. 2020 Jan 14;16(4):682-693. doi: 10.7150/ijbs.37592. PMID: 32025215; PMCID: PMC6990918.

2. Shi F, Zhang J, Liu H, Wu L, Jiang H, Wu Q, Liu T, Lou M, Wu H. The dual PI3K/mTOR inhibitor dactolisib elicits anti-tumor activity in vitro and in vivo. Oncotarget. 2017 Dec 9;9(1):706-717. doi: 10.18632/oncotarget.23091. Erratum in: Oncotarget. 2018 Mar 30;9(24):17255. PMID: 29416647; PMCID: PMC5787502.

7. Bioactivity

Biological target:

Dactolisib Tosylate (BEZ235 Tosylate) is a dual PI3K and mTOR kinase inhibitor with IC50 values of 4, 75, 7, 5 nM for PI3Kα, β, γ, δ, respectively.

In vitro activity

BEZ235 reduced cell viability in a dose-dependent manner, as shown by CCK8 assays (Figure 1A). The IC50 values of BEZ235 for HL-60/VCR and K562/ADR cells were 66.69 nmol/L and 71.44 nmol/L, respectively. After treatment with different concentrations of BEZ235 for 24 h, the migration of both cell lines significantly decreased (Figure 1B). BEZ235 also induced apoptosis in the HL60/VCR and K562/ADR cells in a dose-dependent manner (Figure 1C).

Reference: Acta Pharmacol Sin. 2017 Mar; 38(3): 382–391. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5342661/

In vivo activity

Subsequently, the peeled tumors were subjected to paraffin embedded sections. The protein expressions of p53 and p21 in tumor sections were tested by IHC assays. In both K1 and C643 tumors, p21 expression was higher in NVP-BEZ235 treated mice compared with the controls, since an increased percent and stronger staining of p21 positive cells were observed. While only the mice bearing K1 tumors displayed greater portion and stronger staining of p53 positive cells, rather than C643 tumors. These results suggested a p53-independent mechanism of p21 up-regulation in NVP-BEZ235 treated C643 xenograft tumors, which was consistent with the results of in-vitro studies. Moreover, the mitotic cell marker, Ki67 was shown much weaker in the NVP-BEZ235 treated tumors than the control tumors, further suggested NVP-BEZ235 suppresses thyroid cancer cell proliferation (Figure 7C). Taken together, these results indicated that NVP-BEZ235 treatment inhibited tumor growth in mice injected with K1 cells or C643 cells and substantiate our findings that NVP-BEZ235 inhibits thyroid cancer growth independent of TP53 status.

Reference: Int J Biol Sci. 2020; 16(4): 682–693. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6990918/

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.