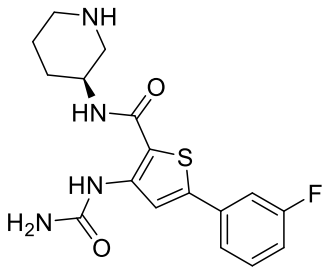
Product data sheet

MedKoo Cat#: 200311 Name: AZD-7762 CAS#: 860352-01-8 (free base) Chemical Formula: $C_{17}H_{19}FN_4O_2S$ Exact Mass: 362.12127 Molecular Weight: 362.42	
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:
AZD-7762 is a synthetic small molecule inhibitor of checkpoint kinases (Chks) with potential chemosensitizing activity. AZD7762 binds to and inhibits Chks, which may prevent cell cycle arrest and subsequent nucleotide excision repair in DNA-damaged tumor cells, resulting in tumor cell apoptosis. This agent may enhance the cytotoxicity of DNA-damaging agents. Chks are protein kinases that regulate either G1/S or G2/M transitions in the cell cycle. In the presence of DNA damage or incomplete DNA replication, Chks become activated and initiate cell cycle arrest to allow DNA repair or the completion of DNA replication.

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	60.67	167.40
DMF	20.0	55.18
Ethanol	10.0	27.59
PBS (pH 7.2)	10.0	27.59

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.76 mL	13.80 mL	27.59 mL
5 mM	0.55 mL	2.76 mL	5.52 mL
10 mM	0.28 mL	1.38 mL	2.76 mL
50 mM	0.06 mL	0.28 mL	0.55 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. Zhu J, Zou H, Yu W, Huang Y, Liu B, Li T, Liang C, Tao H. Checkpoint kinase inhibitor AZD7762 enhance cisplatin-induced apoptosis in osteosarcoma cells. Cancer Cell Int. 2019 Jul 27;19:195. doi: 10.1186/s12935-019-0896-9. PMID: 31372095; PMCID: PMC6660702.
2. Park YH, Kim DK, Kim HW, Kim HS, Lee D, Lee MB, Min KY, Koo J, Kim SJ, Kang C, Kim YM, Kim HS, Choi WS. Repositioning of anti-cancer drug candidate, AZD7762, to an anti-allergic drug suppressing IgE-mediated mast cells and allergic responses via the inhibition of Lyn and Fyn. Biochem Pharmacol. 2018 Aug;154:270-277. doi: 10.1016/j.bcp.2018.05.012. Epub 2018 May 17. PMID: 29777684.

In vivo study

Product data sheet

1. Wang L, Wang Y, Chen A, Jalali A, Liu S, Guo Y, Na S, Nakshatri H, Li BY, Yokota H. Effects of a checkpoint kinase inhibitor, AZD7762, on tumor suppression and bone remodeling. Int J Oncol. 2018 Sep;53(3):1001-1012. doi: 10.3892/ijo.2018.4481. Epub 2018 Jul 13. PMID: 30015873; PMCID: PMC6065446.
2. Park JS, Lee C, Kim HK, Kim D, Son JB, Ko E, Cho JH, Kim ND, Nan HY, Kim CY, Yoon S, Lee SH, Choi HG. Suppression of the metastatic spread of breast cancer by DN10764 (AZD7762)-mediated inhibition of AXL signaling. Oncotarget. 2016 Dec 13;7(50):83308-83318. doi: 10.18632/oncotarget.13088. PMID: 27829217; PMCID: PMC5347771.

7. Bioactivity

Biological target:

AZD-7762 is a potent ATP-competitive checkpoint kinase (Chk) inhibitor in with an IC50 of 5 nM for Chk1.

In vitro activity

As shown in Fig. 1a, MTS assay showed that AZD7762 had no significant inhibitory effect on the proliferation of human osteosarcoma cell lines at low concentrations (≤ 200 nmol/L), and AZD7762 inhibited the two cell lines at higher concentrations (> 200 nmol/L). The effect appeared dose-dependent. The IC50 of AZD7762 on HOS and Saos-2 cell lines were 550 nmol/L and 2.3 μmol/L on 24 h, respectively. For further experiments, this study determined the concentration of AZD7762 to be 100 nmol/L based on the results of MTS and according to the referenced literature. At this concentration, AZD7762 had no significant inhibitory effect on the two osteosarcoma cell lines.

Reference: Cancer Cell Int. 2019; 19: 195. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6660702/

In vivo activity

As shown in the orthotopic metastasis model using 4T1 cell line (a mouse breast cancer cell line) carrying luciferase gene, DN10764 treatment significantly suppressed the progression of growth (Figure 6C) as well as lung metastasis (Figure 6D) in a dose-dependent manner. These results were further confirmed in another metastasis model, in which mice were pre-pretreated with DN10764 2 h prior to the injection of MDA-MB-231-luc2-tdTomato cells into the arterial circulation of nude mice via intracardiac injection. As shown in Supplementary Figure S4, compared with vehicle-injected mice, the average bioluminescence at day 43 decreased by 24% or 40% for mice treated with 10 or 20 mg/kg DN1076, respectively. Two dosing regimens (10 mg/kg and 20 mg/kg) did not affect the average animal body weight compared with vehicle groups (Figure 6B and Supplementary Figure S4B). Taken together, these results clearly demonstrated that DN10764 suppressed in vivo tumor progression and metastasis of breast cancer cells.

Reference: Oncotarget. 2016 Dec 13; 7(50): 83308–83318. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5347771/