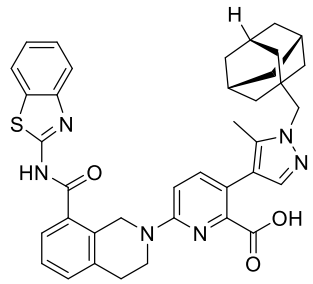
Product data sheet

MedKoo Cat#: 406841 Name: A-1331852 CAS#: 1430844-80-6 Chemical Formula: $C_{38}H_{38}N_6O_3S$ Exact Mass: 658.2726 Molecular Weight: 658.82	
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:
A-1331852 is a potent BCL-XL-selective inhibitor. BCL-XL is the major antiapoptotic survival protein and may be a novel therapeutic target in CML. BCL-XL-selective inhibitors have the potential to enhance the efficacy of docetaxel in solid tumors and avoid the exacerbation of neutropenia observed with navitoclax. A-1331852 may have potential as an improved cancer therapeutic.

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	76.0	115.45
DMF	5.0	7.59
DMF:PBS (pH 7.2) (1:3)	0.25	0.38

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.52 mL	7.59 mL	15.18 mL
5 mM	0.30 mL	1.52 mL	3.04 mL
10 mM	0.15 mL	0.76 mL	1.52 mL
50 mM	0.03 mL	0.15 mL	0.30 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. Wang L, Doherty GA, Judd AS, Tao ZF, Hansen TM, Frey RR, Song X, Bruncko M, Kunzer AR, Wang X, Wendt MD, Flygare JA, Catron ND, Judge RA, Park CH, Shekhar S, Phillips DC, Nimmer P, Smith ML, Tahir SK, Xiao Y, Xue J, Zhang H, Le PN, Mitten MJ, Boghaert ER, Gao W, Kovar P, Choo EF, Diaz D, Fairbrother WJ, Elmore SW, Sampath D, Leverson JD, Souers AJ. Discovery of A-1331852, a First-in-Class, Potent, and Orally-Bioavailable BCL-XL Inhibitor. ACS Med Chem Lett. 2020 Mar 30;11(10):1829-1836. doi: 10.1021/acsmedchemlett.9b00568. PMID: 33062160; PMCID: PMC7549103.

In vivo study

1. Sejic N, George LC, Tierney RJ, Chang C, Kondrashova O, MacKinnon RN, Lan P, Bell AI, Lessene G, Long HM, Strasser A, Shannon-Lowe C, Kelly GL. BCL-XL inhibition by BH3-mimetic drugs induces apoptosis in models of Epstein-Barr virus-associated T/NK-cell lymphoma. Blood Adv. 2020 Oct 13;4(19):4775-4787. doi: 10.1182/bloodadvances.2020002446. PMID: 33017468; PMCID: PMC7556124.

7. Bioactivity

Product data sheet

Biological target:

A-1331852 is a BCL-XL selective inhibitor with a Ki of less than 10 pM.

In vitro activity

The cell-killing efficacy of A-1331852 against MOLT-4 cells was improved by 10- to 30-fold relative to the cyclohexane 12, while maintaining selectivity against the RS4;11 cell line. Thus, A-1331852 exhibited a 6 nM EC50 against the MOLT-4 cell line, a level of in vitro efficacy 20-fold more potent than our previously disclosed tool compound A-1155463. The mechanism-based effects of A-1331852 in MOLT-4 cells were rigorously established, as reported previously. Specifically, treatment of these tumor cells with A-1331852 disrupted BCL-XL:BIM complexes and induced classical features of apoptosis including cytochrome c release, caspase-3/-7 activation, and externalization of phosphatidylserine as determined by flow cytometric evaluation of Annexin-V staining.

Reference: ACS Med Chem Lett. 2020 Oct 8; 11(10): 1829–1836. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7549103/

In vivo activity

In NSG mice intraperitoneally injected with SNK6 cells (SNK6-IP mice), a significant delay in tumor development was observed after treatment with A-1331852 compared with vehicle-treated mice, with median tumor latencies of 56 days and 37 days posttransplant, respectively (P = .0002) (Figure 4A). Similarly, in SNK6-SC–bearing mice, A-1331852 treatment significantly delayed tumor growth (median tumor latency of 56 days compared with vehicle-treated mice (37 days) (P = .022)) (Figure 4B). In contrast, A-1331852 was ineffective at delaying tumor growth in mice transplanted with SNT15 cells (Figure 4C) or MEC04 cells (Figure 4D). Following drug treatment (day 14), there was a marked decrease in platelet numbers, consistent with successful administration of the drug with BCL-XL inhibition causing on-target thrombocytopenia (Figure 4A,D).59 As expected, the platelet counts rebounded to pretreatment levels by the time of sacrifice (days 34-62 posttransplant).

Reference: Blood Adv. 2020 Oct 13; 4(19): 4775–4787. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7556124/

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.