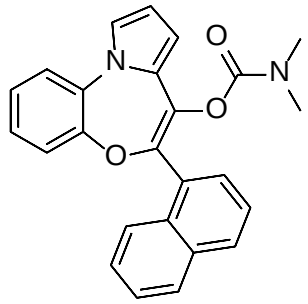
Product data sheet

MedKoo Cat#: 531390 Name: PBOX-6 CAS: 290814-68-5 Chemical Formula: $C_{25}H_{20}N_2O_3$ Exact Mass: 396.1474 Molecular Weight: 396.446	
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:

PBOX-6 belongs to a group of tubulin-targeting pyrrolo-1,5-benzoxazepine (PBOX) compounds that potently induce apoptosis in a wide spectrum of cancer cells, including those originating from the four main types of leukemia and those exhibiting multi-drug resistance (IC50 = 2.28 μM/HL60-MDR1, 2.86 μM/HL60-BCG2, 1.91 μM/HL60; IC50 = 4.71 μM/A2780-ADR, 4.10 μM/A2780). PBOX-6 inhibits the assembly of purified tubulin in cell-free assays and causes microtubule depolymerization in MCF-7 cells by binding a tubulin site distinct from those targeted by vinblastine and colchicine. When administered via intratumoral injection (7.5 mg/kg/day) in vivo, PBOX-6 is reported to significantly inhibit tumour growth in a murine model of neuroblastoma and a CML model of the imatinib-resistant T315I mutants.

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	33.33	84.07

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.52 mL	12.61 mL	25.22 mL
5 mM	0.50 mL	2.52 mL	5.04 mL
10 mM	0.25 mL	1.26 mL	2.52 mL
50 mM	0.05 mL	0.25 mL	0.50 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. Mc Gee MM, Hyland E, Campiani G, Ramunno A, Nacci V, Zisterer DM. Caspase-3 is not essential for DNA fragmentation in MCF-7 cells during apoptosis induced by the pyrrolo-1,5-benzoxazepine, PBOX-6. FEBS Lett. 2002 Mar 27;515(1-3):66-70. doi: 10.1016/s0014-5793(02)02440-7. PMID: 11943196.
2. Zisterer DM, Campiani G, Nacci V, Williams DC. Pyrrolo-1,5-benzoxazepines induce apoptosis in HL-60, Jurkat, and Hut-78 cells: a new class of apoptotic agents. J Pharmacol Exp Ther. 2000 Apr;293(1):48-59. PMID: 10734152.

In vivo study

1. Bright SA, McElligott AM, O'Connell JW, O'Connor L, Carroll P, Campiani G, Deininger MW, Conneally E, Lawler M, Williams DC, Zisterer DM. Novel pyrrolo-1,5-benzoxazepine compounds display significant activity against resistant chronic myeloid leukaemia cells in vitro, in ex vivo patient samples and in vivo. Br J Cancer. 2010 May 11;102(10):1474-82. doi: 10.1038/sj.bjc.6605670. Epub 2010 Apr 20. PMID: 20407438; PMCID: PMC2869169.

2. Greene LM, Fleeton M, Mulligan J, Gowda C, Sheahan BJ, Atkins GJ, Campiani G, Nacci V, Lawler M, Williams DC, Zisterer DM. The pyrrolo-1,5-benzoxazepine, PBOX-6, inhibits the growth of breast cancer cells in vitro independent of estrogen receptor status and inhibits breast tumour growth in vivo. Oncol Rep. 2005 Nov;14(5):1357-63. PMID: 16211309.

7. Bioactivity

Biological target:

PBOX 6 is a pyrrolo-1,5-benzoxazepine (PBOX) compound, acts as a microtubule-depolymerizing agent and an apoptotic agent.

In vitro activity

PBOX-6, a potent member of the series, caused activation of a member of the caspase-3 family of proteases. In addition, the caspase-3-like inhibitor z-DEVD-fmk, but not the caspase-1-like inhibitor z-YVAD-fmk prevented PBOX-6-induced apoptosis, suggesting that caspase 3-like proteases are involved in the mechanism by which PBOX compounds induce apoptosis. The release of cytochrome c into the cytosol in HL-60 cells in response to PBOX-6 suggests that this cellular response may be important in the mechanism by which PBOX-6 induces apoptosis.

Reference: J Pharmacol Exp Ther. 2000 Apr;293(1):48-59. https://pubmed.ncbi.nlm.nih.gov/10734152/

In vivo activity

Injections were initiated on day 8 when there was no significant difference in tumour volume between the control and the PBOX-treated groups. By day 10, PBOX-6 had significantly reduced tumour growth when compared to control group. At the experimental end point, day 18, mice were killed by CO_2 asphyxiation and a splenectomy was performed. The vehicle-treated group showed gross enlargement of spleens, or splenomegaly a clinical symptom of advanced disease, when compared to the PBOX-6-treated group, with a 3.7-fold increase in weight from 163.3±39.51 to 608.7±105.3 mg (*P*-value: 0.0027,**) (Figure 4C). This is likely to be due to the reduced tumour burden of PBOX-treated animals.

Reference: Br J Cancer. 2010 May 11;102(10):1474-82. https://pubmed.ncbi.nlm.nih.gov/20407438/

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.