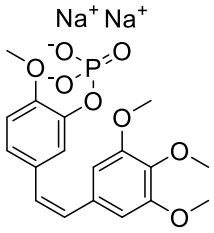
Product data sheet

MedKoo Cat#: 200800 Name: Fosbretabulin disodium CAS#: 168555-66-6 (disodium) Chemical Formula: $C_{18}H_{19}Na_2O_8P$ Molecular Weight: 440.29	
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:

Fosbretabulin disodium is the disodium salt of a water-soluble phosphate derivative of a natural stilbenoid phenol derived from the African bush willow (Combretum caffrum) with potential vascular disrupting and antineoplastic activities. Upon administration, the prodrug fosbretabulin is dephosphorylated to its active metabolite, the microtubule-depolymerizing agent combretastatin A4, which binds to tubulin dimers and prevents microtubule polymerization, resulting in mitotic arrest and apoptosis in endothelial cells. In addition, this agent disrupts the engagement of the endothelial cell–specific junctional molecule vascular endothelial-cadherin (VE-cadherin) and so the activity of the VE-cadherin/β-catenin/Akt signaling pathway, which may result in the inhibition of endothelial cell migration and capillary tube formation. As a result of fosbretabulin's dual mechanism of action, the tumor vasculature collapses, resulting in reduced tumor blood flow and ischemic necrosis of tumor tissue.

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
DMF	1.0	2.27
PBS (pH 7.2)	5.0	11.36
Water	4.5	10.22

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.27 mL	11.36 mL	22.71 mL
5 mM	0.45 mL	2.27 mL	4.54 mL
10 mM	0.23 mL	1.14 mL	2.27 mL
50 mM	0.05 mL	0.23 mL	0.45 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

Signoretto E, Bissinger R, Castagna M, Lang F. Stimulation of Eryptosis by Combretastatin A4 Phosphate Disodium (CA4P). Cell Physiol Biochem. 2016;38(3):969-81. doi: 10.1159/000443049. Epub 2016 Mar 4. PMID: 26938611.

In vivo study

1. Tochinai R, Komatsu K, Murakami J, Nagata Y, Ando M, Hata C, Suzuki T, Kado S, Kobayashi T, Kuwahara M. Histopathological and functional changes in a single-dose model of combretastatin A4 disodium phosphate-induced myocardial damage in rats. J Toxicol Pathol. 2018 Oct;31(4):307-313. doi: 10.1293/tox.2018-0023. Epub 2018 Aug 5. PMID: 30393435; PMCID: PMC6206283.
2. Ley CD, Horsman MR, Kristjansen PE. Early effects of combretastatin-A4 disodium phosphate on tumor perfusion and interstitial fluid pressure. Neoplasia. 2007 Feb;9(2):108-12. doi: 10.1593/neo.06733. PMID: 17356706; PMCID: PMC1813937.

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7. Bioactivity

Biological target:

Fosbretabulin disodium is a tubulin destabilizing agent that selectively targets endothelial cells.

In vitro activity

The present observations reveal a novel effect of CA4P (Fosbretabulin disodium), i.e. the triggering of suicidal erythrocyte death or eryptosis. Exposure of human erythrocytes to CA4P results in cell shrinkage and cell membrane scrambling with phosphatidylserine translocation to the erythrocyte surface. The CA4P concentrations required for the stimulation of eryptosis are in the range of concentrations encountered in the plasma of patients. The higher concentrations employed here (50 and 100 µM) would be approached, however, only following intake of toxic drug doses.

Reference: Cell Physiol Biochem. 2016; 38(3): 969-81. https://air.unimi.it/handle/2434/391841#.YK_V9ahKiUk

In vivo activity

At 0.5 h after dosing, decreases in HR, EF, and CO and increases in plasma CK, CK-MB, and FABP3 were detected in CA4DP (Fosbretabulin disodium)-treated rats. Meanwhile, slight histopathological changes in the myocardium and capillary were observed, but changes in HR and EF were not obvious at 24 h after dosing. At 72 h after dosing, severe histopathological changes in the myocardium were observed, and decreases in HR, EF, and CO recurred. These results suggested that CA4DP-induced cardiac events in rats had occurred within a few minutes and recovered temporarily at 24 h along with the decreases in blood level of CA4DP. Progression of necrosis and inflammation in addition to deterioration of general condition might induce decreases in HR, EF, and CO again.

Reference: J Toxicol Pathol. 2018 Oct; 31(4): 307–313. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6206283/

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.