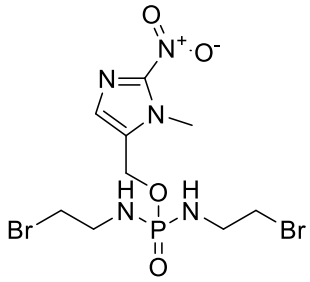
Product data sheet

MedKoo Cat#: 202901 Name: Evofosfamide CAS#: 918633-87-1 Chemical Formula: $C_9H_{16}Br_2N_5O_4P$ Exact Mass: 446.93067 Molecular Weight: 449.04	
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:
Evofosfamide, also known as TH-302, is a hypoxia-activated prodrug consisting of a 2-nitroimidazole phosphoramidate conjugate with potential antineoplastic activity. The 2-nitroimidazole moiety of hypoxia-activated prodrug TH-302 acts as a hypoxic trigger, releasing the DNA-alkylating dibromo isophosphoramide mustard moiety within hypoxic regions of tumors. Normoxic tissues may be spared due to the hypoxia-specific activity of this agent, potentially reducing systemic toxicity. Check for active clinical trials or closed clinical trials using this agent. (NCI).

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	90	200.43
Ethanol	90	200.43
Water	10	22.27

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.23 mL	11.13 mL	22.27 mL
5 mM	0.45 mL	2.23 mL	4.45 mL
10 mM	0.22 mL	1.11 mL	2.23 mL
50 mM	0.04 mL	0.22 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

1. Meng F, Evans JW, Bhupathi D, Banica M, Lan L, Lorente G, Duan JX, Cai X, Mowday AM, Guise CP, Maroz A, Anderson RF, Patterson AV, Stachelek GC, Glazer PM, Matteucci MD, Hart CP. Molecular and cellular pharmacology of the hypoxia-activated prodrug TH-302. Mol Cancer Ther. 2012 Mar;11(3):740-51. doi: 10.1158/1535-7163.MCT-11-0634. Epub 2011 Dec 6. PMID: 22147748.

In vivo study

1. Zhang X, Wojtkowiak JW, Martinez GV, Cornnell HH, Hart CP, Baker AF, Gillies R. MR Imaging Biomarkers to Monitor Early Response to Hypoxia-Activated Prodrug TH-302 in Pancreatic Cancer Xenografts. PLoS One. 2016 May 26;11(5):e0155289. doi: 10.1371/journal.pone.0155289. PMID: 27227903; PMCID: PMC4882075.

7. Bioactivity
Biological target:

Product data sheet

Evofosfamide (TH-302) is a hypoxia-activated prodrug with IC50 of 10 μM and 1000 μM in hypoxia (N2) and normoxia (21% O2), respectively.

In vitro activity

Enhanced TH-302 cytotoxicity under hypoxia was observed across 32 human cancer cell lines. One-electron reductive enzyme dependence was confirmed using cells overexpressing human NADPH:cytochrome P450 oxidoreductase and radiolytic reduction established the single-electron stoichiometry of TH-302 fragmentation (activation). Examining downstream effects of TH-302 activity, it was observed that hypoxia-dependent induction of γH2AX phosphorylation, DNA cross-linking, and cell-cycle arrest. Chinese hamster ovary cell-based DNA repair mutant cell lines were used. Lines deficient in homology-dependent repair, but not lines deficient in base excision, nucleotide excision, or nonhomologous end-joining repair, exhibited marked sensitivity to TH-302 under hypoxia. Consistent with this finding, enhanced sensitivity to TH-302 was also observed in lines deficient in BRCA1, BRCA2, and FANCA. Finally, TH-302 activity in the three-dimensional tumor spheroid and multicellular layer models was characterized. TH-302 showed much enhanced potency in H460 spheroids compared with H460 monolayer cells under normoxia. Multicellular layers composed of mixtures of parental HCT116 cells and HCT116 cells engineered to express an oxygen-insensitive bacterial nitroreductase showed that TH-302 exhibits a significant bystander effect.

Reference: Mol Cancer Ther. 2012 Mar;11(3):740-51. http://mct.aacrjournals.org/cgi/pmidlookup?view=long&pmid=22147748

In vivo activity

Three human PDAC xenografts with known differential responses to TH-302 were imaged prior to, and at 24 h and 48 hours following a single dose of TH-302 or vehicle to determine if imaging changes presaged changes in tumor volumes. DW-MRI was performed at five b-values to generate apparent diffusion coefficient of water (ADC) maps. For DCE-MRI, a standard clinically available contrast reagent, Gd-DTPA, was used to determine blood flow into the tumor region of interest. TH-302 induced a dramatic decrease in the DCE transfer constant (Ktrans) within 48 hours after treatment in the sensitive tumors, Hs766t and Mia PaCa-2, whereas TH-302 had no effect on the perfusion behavior of resistant SU.86.86 tumors.

Reference: PLoS One. 2016 May 26;11(5):e0155289. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/27227903/

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.