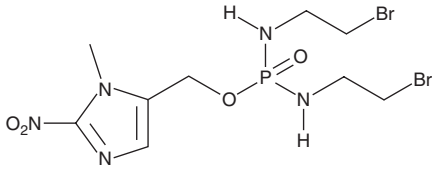
PRODUCT INFORMATION

TH-302

Item No. 22195

CAS Registry No.: 918633-87-1
Formal Name: N,N'-*bis*(2-bromoethyl)-phosphorodiamidic acid, (1-methyl-2-nitro-1H-imidazol-5-yl)methyl ester
Synonym: Evofosfamide
MF: $C_9H_{16}Br_2N_5O_4P$
FW: 449.0
Purity: ≥95%
UV/Vis.: λ_{max}: 314 nm
Supplied as: A crystalline solid
Storage: -20°C
Stability: ≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

TH-302 is supplied as a crystalline solid. A stock solution may be made by dissolving the TH-302 in the solvent of choice. TH-302 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide, which should be purged with an inert gas. The solubility of TH-302 in these solvents is approximately 30 mg/ml.

Further dilutions of the stock solution into aqueous buffers or isotonic saline should be made prior to performing biological experiments. Ensure that the residual amount of organic solvent is insignificant, since organic solvents may have physiological effects at low concentrations. Organic solvent-free aqueous solutions of TH-302 can be prepared by directly dissolving the crystalline solid in aqueous buffers. The solubility of TH-302 in PBS, pH 7.2, is approximately 0.3 mg/ml. We do not recommend storing the aqueous solution for more than one day.

Description

TH-302 is a hypoxia-activated prodrug and DNA alkylating agent with anticancer activity.[1] It is selectively cytotoxic to H460 human non-small cell lung cancer (NSCLC) cells grown under hypoxic over normoxic conditions (IC_{50}s = 0.019 and 5.1 µM, respectively).[1] Under hypoxic conditions, TH-302 undergoes a one-electron reduction to form an active radical intermediate that is then further reduced to form a DNA-intercalating hydroxylamine. Under normoxic conditions, the radical intermediate is quenched and induces reformation of the inactive nitroazole prodrug. TH-302 reduces survival of H460 and HT-29 cells in a clonogenic assay (IC_{50}s = 0.2 and 0.2 µM, respectively). *In vivo*, TH-302 (33 mg/kg per day) inhibits primary tumor growth by 41% in an MIA PaCa-2-RFP mouse orthotopic xenograft model. It inhibits tumor growth by greater than 40% in Calu-6 NSCLC, H82 small cell lung, A375 melanoma, PC-3 prostate, and BxPC-3 pancreatic cancer mouse xenograft models when administered at 50 mg/kg.[2]

References

1. Duan, J.-X., Jiao, H., Kaizerman, J., *et al.* Potent and highly selective hypoxia-activated achiral phosphoramidate mustards as anticancer drugs. *J. Med. Chem.* **51(8)**, 2412-2420 (2008).
2. Sun, J.D., Liu, Q., Wang, J., *et al.* Selective tumor hypoxia targeting by hypoxia-activated prodrug TH-302 inhibits tumor growth in preclinical models of cancer. *Clin. Cancer Res.* **18(3)**, 758-770 (2012).

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