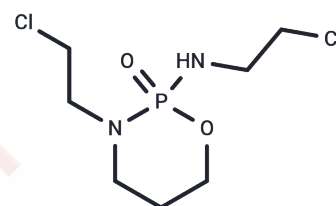


Ifosfamide

Chemical Properties

CAS No. :	3778-73-2
Formula:	C7H15Cl2N2O2P
Molecular Weight:	261.09
Storage:	Powder: -20°C for 3 years In solvent: -80°C for 1 year Actual storage temperature shall be subject to the COA.



Biological Description

Description	Ifosfamide (NSC-109724) alkylates and forms DNA crosslinks, thereby preventing DNA strand separation and DNA replication. Ifosfamide is a synthetic analog of the nitrogen mustard cyclophosphamide with antineoplastic activity. This agent is a prodrug that must be activated through hydroxylation by hepatic microsomal enzymes.
Targets(IC50)	DNA Alkylator/Crosslinker,DNA/RNA Synthesis
In vitro	Ifosfamide induced bladder edema, which peaked 12 hours after Ifosfamide injection. Microscopic analysis showed vascular congestion, edema, hemorrhage, fibrin deposition, neutrophil infiltration and epithelial denudation. Inducible nitric oxide synthase immunoreactivity was strongly reactive in the cytoplasm of bladder epithelial cells, and diffuse necrosis was seen. Intraperitoneal administration of 100 mg/kg, 200 mg/kg and 400 mg/kg Ifosfamide to mice induced a dose-dependent increase in bladder wet weight and Evans blue extravasation. Pretreatment with mesna reduced the increase in bladder edema, whereas treatment with l - ng -nitroarginine methyl ester, antisera TNF-alpha or IL-1beta, thalidomide, or pentoxifylline inhibited bladder edema and microscopic changes. Antiserum treatment also inhibited the expression of inducible nitric oxide synthase within the uroepithelium. Nitric oxide produced by inducible nitric oxide synthase was involved in uroepithelial cell injury and in the inflammatory response leading to hemorrhagic cystitis after ifosfamide administration in mice.
In vivo	In the liver, Ifosfamide it is a prodrug converted to active alkylated compounds by cytochrome P450 mixed function oxidase. Ifosfamide has shown promising antitumor effects in pediatric solid tumors, ovarian cancer, small cell lung cancer, non-Hodgkin's and Hodgkin's lymphomas.Ifosfamide (50 mM) increases the levels of CYP2C8/9, CYP3A4 proteins in hepatocytes, which in turn elevates the rate of 4-hydroxylation of the hepatocytes themselves. In hepatocytes with higher CYP3A4 expression than CYP3A5, Ifosfamide induced only CYP3A4 expression.Ifosfamide was highly cytotoxic to MCF-7 cells stably transfected with CYP2B1 (which could be significantly reduced by the CYP2B1 inhibitor, metipraminexone), but did not affect the expression of β -galactosidase and the pro-tumor cells of MCF- 7 cells. In the prevention of tumor recurrence, the combination of Ifosfamide and zoledronic acid was more effective than the drug alone in increasing bone formation and improving tissue repair.
Kinase Assay	cAMP kinase assay: Diced epididymal fat pads from fed Wistar rats (175-225 gm) are obtained after decapitation and incubated at 37 °C for two hours in Krebs-bicarbonate

Kinase Assay	buffer containing 1.27 mM CaCl ₂ . When added, Tolbutamide is present only during the incubation. After incubation fat pads are rinsed and sonicated in cold Krebs-bicarbonate buffer. The aqueous supernatants from centrifugation at 50,000 × g for 30 minutes at 4 °C contained 0.75 to 1.25 mg protein per mL and are assayed for cyclic AMP-stimulated protein kinase activity. The assay is performed in 0.2 mL with these additions, 10 μmoles sodium glycerofosphate pH 7.0, 2 μmoles sodium fluoride, 0.4 μmoles theophylline, 0.1 μmoles ethylene glycol bis (β-aminoethyl ether)-N, N'-tetraacetic acid, 3 μmoles magnesium chloride, 0.3 mg mixed histone, 2 nmoles (γ- 32P) ATP, 1 nmoles cyclic AMP when indicated, and 0.05 ml of supernatant.
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Solubility Information

Solubility	H ₂ O: 48 mg/mL (183.84 mM),Sonication is recommended. DMSO: 250 mg/mL (957.52 mM),Sonication is recommended. Ethanol: 49 mg/mL (187.67 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (7.66 mM),Sonication is recommended. <i>Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.</i>

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	3.8301 mL	19.1505 mL	38.301 mL
5 mM	0.766 mL	3.8301 mL	7.6602 mL
10 mM	0.383 mL	1.915 mL	3.8301 mL
50 mM	0.0766 mL	0.383 mL	0.766 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

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- Helal M. Prenatal effects of transplacental exposure to ifosfamide in rats. Biotech Histochem. 2016 Jul;91(5):357-68.

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