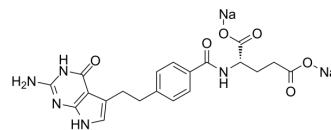


Pemetrexed disodium

Cat. No.:	HY-10820A
CAS No.:	150399-23-8
Molecular Formula:	C ₂₀ H ₁₉ N ₅ Na ₂ O ₆
Molecular Weight:	471.37
Target:	Antifolate; Autophagy; Apoptosis
Pathway:	Cell Cycle/DNA Damage; Autophagy; Apoptosis
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro	H ₂ O : 100 mg/mL (212.15 mM); ultrasonic and warming and heat to 60°C					
	Preparing Stock Solutions	Solvent Concentration	Mass	1 mg	5 mg	10 mg
		1 mM		2.1215 mL	10.6074 mL	21.2148 mL
		5 mM		0.4243 mL	2.1215 mL	4.2430 mL
		10 mM		0.2121 mL	1.0607 mL	2.1215 mL
Please refer to the solubility information to select the appropriate solvent.						
In Vivo	1. Add each solvent one by one: Saline Solubility: 100 mg/mL (212.15 mM); Clear solution; Need ultrasonic					
	2. Add each solvent one by one: PBS Solubility: 50 mg/mL (106.07 mM); Clear solution; Need ultrasonic					

BIOLOGICAL ACTIVITY

Description	Pemetrexed disodium (LY231514 disodium) is an antifolate, the K _i s of the polyglutamated metabolites of Pemetrexed disodium are 1.3, 7.2, and 65 nM for inhibits thymidylate synthase (TS), dihydrofolate reductase (DHFR), and glycinamide ribonucleotide formyltransferase (GARFT), respectively ^[1] .
IC₅₀ & Target	Ki: 1.3 nM (TS), 7.2 nM (DHFR), 65 nM (GARFT) ^[1]
In Vitro	Pemetrexed (LY231514) disodium is a novel classical antifolate, the antitumor activity of which may result from simultaneous and multiple inhibition of several key folate-requiring enzymes via its polyglutamated metabolites. Pemetrexed (LY231514) is one of the best substrates that is known for the enzyme FPGS (K _m =1.6 μM and V _{max} /K _m =621). It is likely that polyglutamation and the polyglutamated metabolites of LY231514 play profound roles in determining both the selectivity and the antitumor activity of this novel agent. Whereas LY231514 only moderately inhibits TS (K _i =340 nM,

recombinant mouse), the pentaglutamate of LY231514 is 100-fold more potent ($K_i=3.4$ nM), making LY231514 one of the most potent folate-based TS inhibitors^[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

The group of mice treated with PC61 plus Pemetrexed demonstrates statistically longer survival than other groups. In a survival analysis, significantly better survival is observed in the group of mice treated with PC61 plus Pemetrexed compared with those treated with PC61 alone, rat IgG plus Pemetrexed, or no treatment^[2].

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PROTOCOL

Cell Assay ^[1]

Dose-response curves are generated to determine the concentration required for 50% inhibition of growth (IC_{50}). Pemetrexed is dissolved initially in DMSO at a concentration of 4 mg/mL and further diluted with cell culture medium to the desired concentration. CCRF-CEM leukemia cells in complete medium are added to 24-well Cluster plates at a final concentration of 4.8×10^4 cells/well in a total volume of 2 mL. Test compounds at various concentrations are added to duplicate wells so that the final volume of DMSO is 0.5%. The plates are incubated for 72 h at 37°C in an atmosphere of 5% CO_2 in air. At the end of the incubation, cell numbers are determined on a ZBI Coulter counter. Control wells usually contain 4×10^5 to 6×10^5 cells at the end of the incubation. For several studies, IC_{50} s are determined for each compound in the presence of either 300 μ M AICA, 5 μ M thymidine, 100 μ M hypoxanthine, or combination of 5 μ M thymidine plus 100 μ M hypoxanthine^[1].

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Animal Administration ^[2]

Mice^[2]

Female CBA mice and female NOD/SCID mice (NOD.CB17-Prkdc^{scid}) at 6-8 wk of age are used. Pemetrexed (100 mg/kg) is given i.p. from days 4-8 (5 consecutive d) to tumor-bearing mice to explore the synergistic effect when combined with anti-CD25 Ab or IgG control. The dose and schedule used for Pemetrexed in the current study is determined based on previous studies in mice.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Mol Cell. 2019 Dec 5;76(5):838-851.e5.
- J Clin Invest. 2021 Aug 2;131(15):e138022.
- Cell Rep Med. 2023 Jan 10;100911.
- Theranostics. 2020 May 15;10(13):6048-6060.
- J Control Release. 2022 Dec 9;353:490-506.

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REFERENCES

[1]. Shih C, et al. LY231514, a pyrrolo[2,3-d]pyrimidine-based antifolate that inhibits multiple folate-requiring enzymes. *Cancer Res.* 1997 Mar 15;57(6):1116-23.

[2]. Anraku M, et al. Synergistic antitumor effects of regulatory T cell blockade combined with pemetrexed in murine malignant mesothelioma. *J Immunol.* 2010 Jul 15;185(2):956-66.

Caution: Product has not been fully validated for medical applications. For research use only.

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