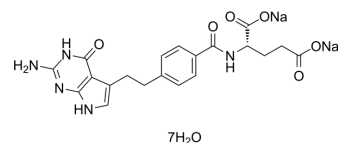


Pemetrexed disodium heptahydrate

Cat. No.:	HY-10820B
CAS No.:	357166-29-1
Molecular Formula:	C ₂₀ H ₂₁ N ₅ O ₆ ·7H ₂ O·2Na
Molecular Weight:	599.5
Target:	Antifolate; Autophagy
Pathway:	Cell Cycle/DNA Damage; Autophagy
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 H₂O : 100 mg/mL (166.81 mM; Need ultrasonic)

Concentration	Solvent	Mass		
		1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	1.6681 mL	8.3403 mL	16.6806 mL
	5 mM	0.3336 mL	1.6681 mL	3.3361 mL
	10 mM	0.1668 mL	0.8340 mL	1.6681 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description Pemetrexed disodium heptahydrate is a novel antifolate, the K_i values of the pentaglutamate of LY231514 are 1.3, 7.2, and 65 nM for inhibits thymidylate synthase (TS), dihydrofolate reductase (DHFR), and glycinamide ribonucleotide formyltransferase (GARFT), respectively.

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 compare

with those treated with PC61 alone, rat IgG plus Pemetrexed, or no treatment^[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay ^[1]

AICARFT inhibition assays are carried out at room temperature by monitoring the formation of [6S]-5,6,7,8-tetrahydrofolate from 10-formyl-[6R,S]-5,6,7,8-tetrahydrofolate at A₂₉₈. All solutions are purged with N₂ gas prior to use. The reaction solution contains 33 mM Tris-Cl, pH 7.4, 25 mM KCl, 5 mM 2-Mercaptoethanol, 0.05 mM AICA ribonucleotide, and 16 nM (2 milliunits/mL) of AICARFT. 10-Formyl-[6R,S]-5,6,7,8-tetrahydrofolate concentrations of 0.037, 0.074, and 0.145 mM are used (0.61, 1.23, and 2.45 times its K_m value, respectively). LY231514 is tested as an inhibitor at 0.08-0.8 mM (four concentrations). When the tri- and pentaglutamates of LY231514 are used as inhibitors, the concentrations are 0.0005-0.009 mM (eight concentrations). Enzyme assays are initiated by the addition of enzyme. Data is analyzed using the ENZFITTER program for competitive inhibition.

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

Cell Assay ^[1]

Dose-response curves are generated to determine the concentration required for 50% inhibition of growth (IC₅₀). 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 4.8×10⁴ 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% CO₂ in air. At the end of the incubation, cell numbers are determined on a ZBI Coulter counter. Control wells usually contain 4×10⁵ to 6×10⁵ cells at the end of the incubation. For several studies, IC₅₀s are determined for each compound in the presence of either 300 μM AICA, 5 μM thymidine, 100 μM hypoxanthine, or combination of 5 μM thymidine plus 100 μM hypoxanthine^[1].

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Animal Administration ^[1]

Dose-response curves are generated to determine the concentration required for 50% inhibition of growth (IC₅₀). 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 4.8×10⁴ 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% CO₂ in air. At the end of the incubation, cell numbers are determined on a ZBI Coulter counter. Control wells usually contain 4×10⁵ to 6×10⁵ cells at the end of the incubation. For several studies, IC₅₀s are determined for each compound in the presence of either 300 μM AICA, 5 μM thymidine, 100 μM hypoxanthine, or combination of 5 μM thymidine plus 100 μM hypoxanthine^[1].

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

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