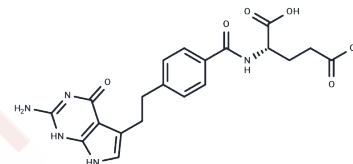


Pemetrexed

Chemical Properties

CAS No. :	137281-23-3
Formula:	C ₂₀ H ₂₁ N ₅ O ₆
Molecular Weight:	427.41
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	Pemetrexed (LY-231514 Disodium Hydrate), a guanine-derived antineoplastic agent, binds to and inhibits the enzyme thymidylate synthase (TS).
Targets(IC50)	Antifolate, Autophagy, DHFR, DNA/RNA Synthesis
In vitro	Pemetrexed (LY231514) disodium is a novel classical antifolate whose antitumor activity likely results from the simultaneous inhibition of several key folate-requiring enzymes via its polyglutamated metabolites. It is one of the best substrates for the enzyme FPGS ($K_m=1.6 \mu\text{M}$, $V_{max}/K_m=621$). Polyglutamation and the polyglutamated metabolites of LY231514 play significant roles in determining its selectivity and antitumor activity. LY231514 only moderately inhibits TS ($K_i=340 \text{ nM}$, recombinant mouse), but its pentaglutamate form is 100-fold more potent ($K_i=3.4 \text{ nM}$), making it one of the most potent folate-based TS inhibitors[1].
In vivo	The group of mice treated with PC61 combined with Pemetrexed exhibited significantly longer survival compared to those treated with PC61 alone, rat IgG combined with Pemetrexed, or left untreated. Survival analysis further confirmed that the PC61 and Pemetrexed combination resulted in significantly improved survival rates [2].
Kinase Assay	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 N ₂ 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.
Cell Research	Pemetrexed is dissolved in DMSO and stored, and then diluted with cell culture medium before use[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

Cell Research	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 μM AICA, 5 μM thymidine, 100 μM hypoxanthine, or combination of 5 μM thymidine plus 100 μM hypoxanthine[1].
---------------	---

Solubility Information

Solubility	DMSO: 35 mg/mL (81.89 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 (4.68 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	2.3397 mL	11.6984 mL	23.3967 mL
5 mM	0.4679 mL	2.3397 mL	4.6793 mL
10 mM	0.234 mL	1.1698 mL	2.3397 mL
50 mM	0.0468 mL	0.234 mL	0.4679 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

- 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.
- 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.

Inhibitor · Natural Compounds · Compound Libraries · Recombinant Proteins

This product is for Research Use Only· Not for Human or Veterinary or Therapeutic Use

Tel:781-999-4286 E_mail:info@targetmol.com Address:34 Washington Street,Wellesley Hills,MA 02481