Pemetrexed disodium

Cat. No.: HY-10820A

CAS No.: 150399-23-8

Molecular Formula: $C_{20}H_{19}N_5Na_2O_6$

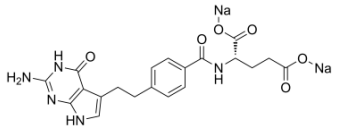
Molecular Weight: 471.37

Target: Antifolate; Autophagy; Apoptosis

Pathway: Cell Cycle/DNA Damage; Autophagy; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

H_2O : ≥ 100 mg/mL (212.15 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Concentration / Solvent / 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.

BIOLOGICAL ACTIVITY

Description

Pemetrexed disodium (LY231514 disodium) is an antifolate, the K_is of the pentaglutamate 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].

IC_{50} & 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 multipie 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 LY23l5l4 only moderately inhibits TS (K_i=340 nM, recombinant mouse), the pentaglutamate of LY23l5l4 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

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 μM AICA, 5 μM thymidine, 100 μM hypoxanthine, or combination of 5 μM hymidine plus 100 μM hypoxanthine[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
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. Premetrexed (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.
- Theranostics. 2020 May 15;10(13):6048-6060.
- Acta Pharmacol Sin. 2021 Jan;42(1):108-114.
- J Mol Med (Berl). 2019 Aug;97(8):1183-1193.
- Beilstein J Org Chem. 2017 Oct 25;13:2252-2263.

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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 malignantmesothelioma. J Immunol. 2010 Jul 15;185(2):956-66.

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

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA