

Product Data Sheet

Product Name: Pemetrexed

Cat. No.: GC11610

Chemical Properties

Cas. No. 150399-23-8

Chemical Name disodium;(2S)-2-[[4-[2-(2-amino-4-oxo-1,7-dihydropyrrolo[2,3-d]pyrimidin-5-yl)ethyl]benzoyl]amino]pentanedioate

SMILES C1=CC(=CC=C1CCC2=CNC3=C2C(=O)N=C(N3)N)C(=O)NC(CCC(=O)[O-])C(=O)[O-].[Na+].[Na+]

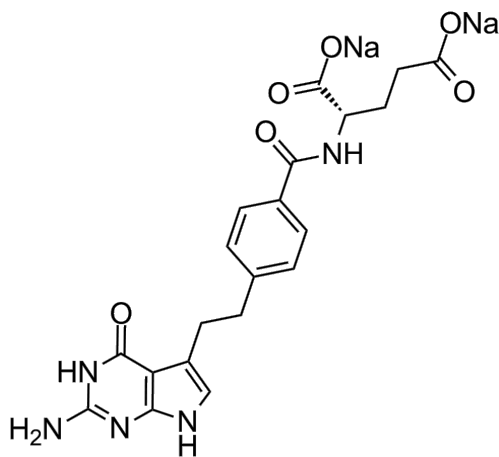
Formula $C_{20}H_{19}N_5Na_2O_6$ M.Wt 471.37

Solubility ≥ 30.67 mg/mL in Water Storage Store at $-20^{\circ}C$

General tips For obtaining a higher solubility, please warm the tube at $37^{\circ}C$ and shake it in the ultrasonic bath for a while. Stock solution can be stored below $-20^{\circ}C$ for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

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**Kinase
experiment:**

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.

Cell experiment:

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 4.8×10^4 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% CO₂ 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, 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 experiment: Mice[2] Female CBA mice and female NOD/SCID mice (NOD.CB17-Prkdcscid) 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 Premetrexed in the current study is determined based on previous studies in mice.

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.

Background

Pemetrexed (also known as pemetrexed disodium) is a novel antifolate antimetabolite targeting multiple enzymes involved in both pyrimidine and purine synthesis. Pemetrexed is an analog of the classic antifolate GARFYT inhibitor lometroxol with a similar chemical structure, where the pyrazine ring in the pterine portion of folic acid and the benzylic nitrogen in the bridge portion of folic acid are replaced by a pyrrole ring and a methylene group respectively. Pemetrexed potently inhibits TS, DHFR, and GARFT as well as AICARFT but with a lesser potency and exhibits antitumor activity in a broad range of tumors, including non-small cell lung carcinoma, malignant mesothelioma, and carcinomas of the breast, colorectum, uterine cervix, head and neck, and bladder.

Reference

- [1]. Luis Paz-Ares, Susana Bezares, Jose M. Tabernero, Daniel Castellanos, and Hernan Cortes-Funes. Review of a promising new agent-pemetrexed disodium. *Cancer* 2003; 97(8 Suppl):2056-2063

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