Product Data Sheet

Product Name: Pralatrexate
Cat. No.: GC12919

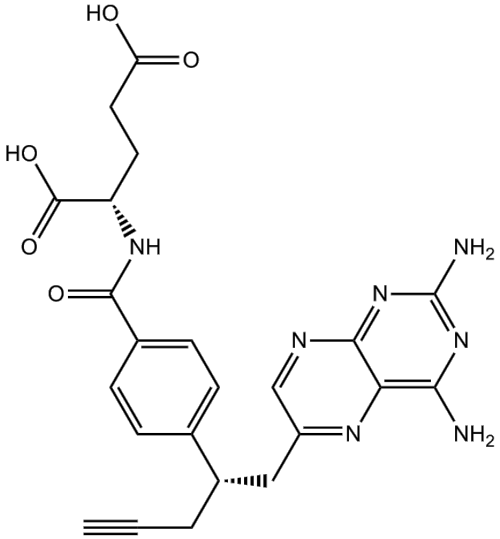
Chemical Properties

Cas. No.	146464-95-1
Chemical Name	(2S)-2-[[4-[1-(2,4-diaminopteridin-6-yl)pent-4-yn-2-yl]benzoyl]amino]pentanedioic acid
SMILES	C#CCC(CC1=CN=C2C(=N1)C(=NC(=N2)N)N)C3=CC=C(C=C3)C(=O)NC(CCC(=O)O)C(=O)O

Formula	$C_{23}H_{23}N_7O_5$	M.Wt	477.47
Solubility	≥ 23.85 mg/mL in DMSO	Storage	Store at -20°C,protect from light

General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°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

Cell experiment [1,2]:

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Cell lines	Cancer cell lines, NCI-H460 human NSCLC cells, MV522 human metastatic human NSCLC cells
Preparation method	The solubility of this compound in DMSO is > 23.9 mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.
Reacting condition	72h
Applications	Pralatrexate showed antiproliferative activity against 15 cancer cell lines with the IC50 values ranged from 0.01 ± 0.002 μM for the prostate cancer cell line PC3 to > 350 μM for the MDA-MB-435 cell line. Pralatrexate dose-dependently inhibited the activity of DHFR. In NCI-H460 cells, treatment with pralatrexate for 15 or 60 min resulted in a short-term uptake of radiolabeled antifolates.

Animal experiment [1]:

Animal models	Female nude mice (nu/nu) bearing NCI-H460 or MV522 tumor cells
Dosage form	Intraperitoneal injection, 1 and 2 mg/kg, every day×5, for two cycles of 5 days

Caution: Product has not been fully validated for medical applications. For research use only.
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Application	In MV522 human non-small cell lung cancer (NSCLC) xenograft, pralatrexate showed increased antitumor activity. In the 2 mg/kg pralatrexate-treated group, the 38% tumor growth inhibition (TGI) was observed. In NCI-H460 NSCLC xenograft, pralatrexate showed antitumor activity in a dose-dependent way. TGI of 1 mg/kg and 2 mg/kg pralatrexate-treated groups was 34% and 52%, respectively. In NCI-H460 and MV522 human tumor xenografts, pralatrexate resulted in dose-dependent weight loss, which suggested its toxicity.
Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

References:

[1]. Izbicka E, Diaz A, Streeper R, et al. Distinct mechanistic activity profile of pralatrexate in comparison to other antifolates in in vitro and in vivo models of human cancers[J]. Cancer chemotherapy and pharmacology, 2009, 64(5): 993-999.

[2]. Serova M, Bieche I, Sablin M P, et al. Single agent and combination studies of pralatrexate and molecular correlates of sensitivity[J]. British journal of cancer, 2011, 104(2): 272.

Background

Pralatrexate is an inhibitor of DHFR with Ki value of 45 nM [1].

Dihydrofolate reductase (DHFR) is an enzyme that reduces dihydrofolic acid to tetrahydrofolic acid, a methyl group shuttle required for the synthesis of purines, thymidylic acid, and certain amino acids.

Pralatrexate is a DHFR inhibitor with high affinity for folylpolyglutamate synthetase (FPGS) and reduced folate carrier 1 (RFC-1), resulting in extensive internalization and accumulation in tumour cells. In 15 human cancer cell lines, pralatrexate showed antiproliferative effects with IC50 < 0.1 μM in PC3, SCC61, DU145, HT29, HOP62, SQ20B, HOP92, HEP2 and IGROV1 cells. While it showed antiproliferative effects with IC50≥ 9 μM in Colo205, HCC2998, MCF7, HCT116, OVCAR3 and MDA-

MB-435 cells [2].

In MV522 human non-small cell lung cancer (NSCLC) xenograft, pralatrexate showed increased antitumor activity. In the 2 mg/kg pralatrexate-treated group, the 38% tumor growth inhibition (TGI) was observed. In NCI-H460 NSCLC xenograft, pralatrexate showed antitumor activity in a dose-dependent way. TGI of 1 mg/kg and 2 mg/kg pralatrexate-treated groups was 34% and 52%, respectively. In the two xenografts, pralatrexate resulted in weight loss, which suggested its toxicity [1].

References:

[1]. Izbicka E, Diaz A, Streeper R, et al. Distinct mechanistic activity profile of pralatrexate in comparison to other antifolates in in vitro and in vivo models of human cancers. Cancer Chemother Pharmacol, 2009, 64(5): 993-999.
[2]. Serova M, Bieche I, Sablin MP, et al. Single agent and combination studies of pralatrexate and molecular correlates of sensitivity. Br J Cancer, 2011, 104(2): 272-280.