Pralatrexate

Cat. No.: HY-10446

CAS No.: 146464-95-1

Molecular Formula: $C_{23}H_{23}N_7O_5$

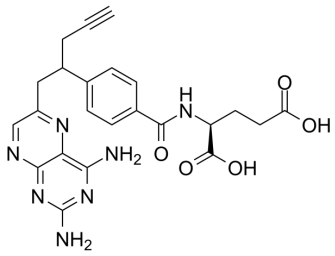
Molecular Weight: 477.47

Target: Antifolate; Apoptosis

Pathway: Cell Cycle/DNA Damage; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (104.72 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0944 mL	10.4719 mL	20.9437 mL
5 mM	0.4189 mL	2.0944 mL	4.1887 mL
10 mM	0.2094 mL	1.0472 mL	2.0944 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.24 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.24 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Pralatrexate is an antifolate and is a potent dihydrofolate reductasean (DHFR) inhibitor with a K_i of 13.4 pM. Pralatrexate is a substrate for folylpolyglutamate synthetase with improved cellular uptake and retention. Pralatrexate has antitumor activities and has the potential for relapsed/refractory T-cell lymphoma treatment[1][2][3][4]. Pralatrexate is a click chemistry reagent, it contains an Alkyne group and can undergo copper-catalyzed azide-alkyne cycloaddition (CuAAc) with molecules containing Azide groups.

IC_{50} & Target

Ki: 13.4 pM (Dihydrofolate reductasean (DHFR))[4]

In Vitro

Pralatrexate (100 pM-200 μM; 48-72 hours; T-lymphoma cell lines) treatment exhibits concentration- and time-dependent

cytotoxicity against a broad panel of T-lymphoma cell lines. The IC_{50} values at 48 and 72 hours, respectively, are as follows: H9 cells, 1.1 nM and 2.5 nM; P12 cells, 1.7 nM and 2.4 nM; CEM cells, 3.2 nM and 4.2 nM; PF-382 cells, 5.5 nM and 2.7 nM; KOPT-K1 cells, 1 nM and 1.7 nM; DND-41 cells, 97.4 nM and 1.2 nM; and HPB-ALL cells, 247.8 nM and 0.77 nM. HH cells are relatively resistant after 48 hours of exposure, with the IC_{50} at 72 hours being 2.8 nM[1].

Pralatrexate (2-5.5 nM; 48-72 hours; H9, HH, P12 and PF382 cells) treatment induces potent apoptosis, and caspase-8 and caspase-9 activation[1].

Pralatrexate (3 nM; 16-48 hours; H9 and P12 cells) treatment clearly increases p27 levels and increases the accumulation of educed folate carrier type 1 (RFC-1) in cells[1].

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

Cell Cytotoxicity Assay[1]

Cell Line:	T-lymphoma cell lines
Concentration:	100 pM-200 μM
Incubation Time:	48 hours, 72 hours
Result:	Exhibited concentration- and time-dependent cytotoxicity against a broad panel of T-lymphoma cell lines.

Apoptosis Analysis[1]

Cell Line:	H9, HH, P12 and PF382 cells
Concentration:	2 nM, 3 nM, 4 nM, 5.5 nM
Incubation Time:	48 hours, 72 hours
Result:	Induced potent apoptosis and caspase activation.

Western Blot Analysis[1]

Cell Line:	H9 and P12 cells
Concentration:	3 nM
Incubation Time:	16 hours, 24 hours, 48 hours
Result:	Clearly increased p27 levels and increased the accumulation of RFC-1 in cells.

In Vivo

The addition of Pralatrexate (15 mg/kg; intraperitoneal injection; on days 1, 4, 8, and 11; SCID-beige mice) to Bortezomib (0.5 mg/kg) enhanced efficacy compared with either drug alone[1].

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

Animal Model:	SCID-beige mice (5-7-week-old) injected with HH cells[1]
Dosage:	15 mg/kg
Administration:	Intraperitoneal injection; on days 1, 4, 8, and 11
Result:	Showed superior efficacy in T-cell malignancies.

CUSTOMER VALIDATION

- Antiviral Res. 2023 Dec 23, 105787.
- Cancers (Basel). 2022 May 20;14(10):2527.
- J Mol Med (Berl). 2019 Aug;97(8):1183-1193.
- Dis Model Mech. 2023 Mar 2;dmm.049769.

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REFERENCES

[1]. Enrica Marchi, et al. Pralatrexate Is Synergistic With the Proteasome Inhibitor Bortezomib in in Vitro and in Vivo Models of T-cell Lymphoid Malignancies. Clin Cancer Res. 2010 Jul 15;16(14):3648-58.

[2]. Francine Foss, et al. Pralatrexate Is an Effective Treatment for Relapsed or Refractory Transformed Mycosis Fungoides: A Subgroup Efficacy Analysis From the PROPEL Study. Clin Lymphoma Myeloma Leuk. 2012 Aug;12(4):238-43.

[3]. Karen Kelly, et al. Randomized Phase 2b Study of Pralatrexate Versus Erlotinib in Patients With Stage IIIB/IV Non-Small-Cell Lung Cancer (NSCLC) After Failure of Prior Platinum-Based Therapy. J Thorac Oncol. 2012 Jun;7(6):1041-8.

[4]. F M Sirotnak, et al. A New Analogue of 10-deazaaminopterin With Markedly Enhanced Curative Effects Against Human Tumor Xenografts in Mice. Cancer Chemother Pharmacol. 1998;42(4):313-8.

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