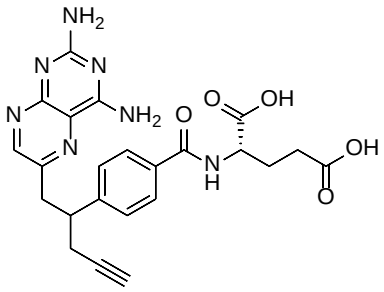
Product data sheet

MedKoo Cat#: 206221 Name: Pralatrexate CAS#: 146464-95-1 (racemic) Chemical Formula: $C_{23}H_{23}N_7O_5$ Exact Mass: 477.1761 Molecular Weight: 477.47	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
Pralatrexate is a folate analogue inhibitor of dihydrofolate reductase (DHFR) exhibiting high affinity for reduced folate carrier-1 (RFC-1) with antineoplastic and immunosuppressive activities. Pralatrexate selectively enters cells expressing RFC-1; intracellularly, this agent is highly polyglutamylated and competes for the folate binding site of DHFR, blocking tetrahydrofolate synthesis, which may result in depletion of nucleotide precursors; inhibition of DNA, RNA and protein synthesis; and apoptotic tumor cell death.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	3.0	6.30

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.09 mL	10.47 mL	20.94 mL
5 mM	0.42 mL	2.09 mL	4.19 mL
10 mM	0.21 mL	1.05 mL	2.09 mL
50 mM	0.04 mL	0.21 mL	0.42 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Kinahan C, Mangone MA, Scotto L, Visentin M, Marchi E, Cho HJ, O'Connor OA. The anti-tumor activity of pralatrexate (PDX) correlates with the expression of RFC and DHFR mRNA in preclinical models of multiple myeloma. Oncotarget. 2020 May 5;11(18):1576-1589. doi: 10.18632/oncotarget.27516. PMID: 32405334; PMCID: PMC7210016.

In vivo study

1. Marchi E, Paoluzzi L, Scotto L, Seshan VE, Zain JM, Zinzani PL, O'Connor OA. 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. doi: 10.1158/1078-0432.CCR-10-0671. Epub 2010 May 25. PMID: 20501616.

7. Bioactivity
Biological target: Pralatrexate is an antifolate and a dihydrofolate reductasean (DHFR) inhibitor with a Ki of 13.4 pM.

In vitro activity

As shown in Figure 3A, MM.1s (multiple myeloma) cells treated with prlatrexate exhibited a distinct pattern of cell cycle events compared to untreated cells as early as 12 hours after exposure to the drug. Pralatrexate treated MM.1s cells accumulated in early

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G1/S phase transition, as demonstrated through 7-AAD and Bromodeoxyuridine (BrdU) co-staining (Figure 3A). Drug-treated MM.1s cells were able to initiate DNA synthesis, visualized as an increase in incorporation of pulsed BrdU (S-phase). However, the cells were unable to progress through S-phase, as visualized as by an increase in BrdU+ diploid (2n) cells. This effect was time and concentration dependent (Figure 3B). The cell cycle analysis of resistant U266 cells was unaltered following treatment with pralatrexate. Across all sensitive cell lines, pralatrexate induced cell cycle arrest in a concentration dependent manner.

Reference: Oncotarget. 2020 May 5;11(18):1576-1589. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7210016/

In vivo activity

The in vivo efficacy of pralatrexate combined with bortezomib was investigated in a xenograft model of cutaneous T-cell lympoma (CTCL). After 30 days from the beginning of the experiment, the results in the combination group treated with pralatrexate at a dose of 15 mg/kg (1/4 of the maximum tolerated dose) and bortezomib given on days 1, 4, 8, and 11 at a dose of 0.5 mg/kg were statistically significant compared with pralatrexate alone (P = 0.002), bortezomib alone (P = 0.001), and the control (P = 0.001; Supplementary Data C). Interestingly, complete responses (CRs) were observed only in the combination cohort, where 6 of 10 mice experienced CR in the combination cohort at day 18, with two of those CRs being maintained beyond day 30. Neither significant weight loss nor death was observed in any of the cohorts. These data support the in vitro experiments in establishing the superior efficacy of this combination in T-cell malignancies.

Reference: Clin Cancer Res. 2010 Jul 15;16(14):3648-58. https://clincancerres.aacrjournals.org/content/16/14/3648.long