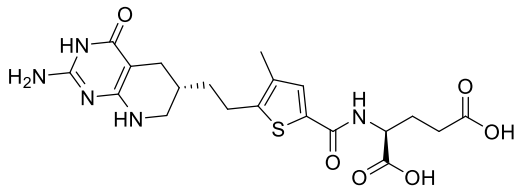
Product data sheet

MedKoo Cat#: 202200 Name: Pelitrexol CAS#: 446022-33-9 Chemical Formula: $C_{20}H_{25}N_5O_6S$ Exact Mass: 463.15255 Molecular Weight: 463.51	
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:
Pelitrexol is a GARFT inhibitor, and is also a water soluble antifolate with anti-proliferative activity. Pelitrexol inhibits activity of glycinamide ribonucleotide formyltransferase (GARFT), the first folate-dependent enzyme of the de novo purine synthesis pathway essential for cell proliferation. Enzyme inhibition reduces the purine nucleotides pool required for DNA replication and RNA transcription. As a result, this agent causes cell cycle arrest in S-phase, and ultimately inhibits tumor cell proliferation.

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	25.0	53.9

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.16 mL	10.79 mL	21.57 mL
5 mM	0.43 mL	2.16 mL	4.31 mL
10 mM	0.22 mL	1.08 mL	2.16 mL
50 mM	0.04 mL	0.22 mL	0.43 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. Emmanuel N, Ragunathan S, Shan Q, Wang F, Giannakou A, Huser N, Jin G, Myers J, Abraham RT, Unsal-Kacmaz K. Purine Nucleotide Availability Regulates mTORC1 Activity through the Rheb GTPase. Cell Rep. 2017 Jun 27;19(13):2665-2680. doi: 10.1016/j.celrep.2017.05.043. PMID: 28658616.

In vivo study

1. Emmanuel N, Ragunathan S, Shan Q, Wang F, Giannakou A, Huser N, Jin G, Myers J, Abraham RT, Unsal-Kacmaz K. Purine Nucleotide Availability Regulates mTORC1 Activity through the Rheb GTPase. Cell Rep. 2017 Jun 27;19(13):2665-2680. doi: 10.1016/j.celrep.2017.05.043. PMID: 28658616.

7. Bioactivity
Biological target:

Pelitrexol (AG 2037) is an inhibitor of glycinamide ribonucleotide formyltransferase (GARFT).

In vitro activity

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To further define the effect of AG2037 on Rheb function, myc-tagged Rheb was immunoprecipitated from HEK293T cells treated with AG2037 with a conformation-specific monoclonal antibody that selectively recognizes RhebGTP. The results showed that AG2037 treatment dramatically decreased the ratio of RhebGTP to total Rheb and concomitantly suppressed S6RP and S6K1 phosphorylation (Figure 5B). Again, supplementation of the culture medium with adenine or guanine abrogated the negative effect of AG2037 on RhebGTP abundance in these cells (Figure 5B). AG2037 treatment consistently led to an upward shift in Rheb mobility during SDS-PAGE (Figure 5A).

Reference: Cell Rep. 2017 Jun 27;19(13):2665-2680. https://linkinghub.elsevier.com/retrieve/pii/S2211-1247(17)30685-X

In vivo activity

Mice harboring established, subcutaneous A427 xenografts were treated with either vehicle or AG2037 via intraperitoneal injection. Tumor growth was markedly reduced in the drug-treated animals relative to the vehicle-treated controls (Figure 4E). Tumor growth was suppressed by 64% and 69% at the 10 mg/kg and 20 mg/kg dosage levels, respectively. In a parallel group of tumor-bearing mice, the effect of AG2037 (20 mg/kg) on mTORC1 signaling 24 hr was assessed after the last drug administration. Immunoblot analyses of excised tumor tissue extracts revealed that AG2037 administration profoundly inhibited mTORC1-dependent phosphorylation of S6K1, S6RP, and CAD (Figure 4F). Thus, inhibition of GARFT-dependent purine biosynthesis blocks mTORC1 functions in this tumor cell line under both tissue culture and in vivo growth conditions.

Reference: Cell Rep. 2017 Jun 27;19(13):2665-2680. https://linkinghub.elsevier.com/retrieve/pii/S2211-1247(17)30685-X