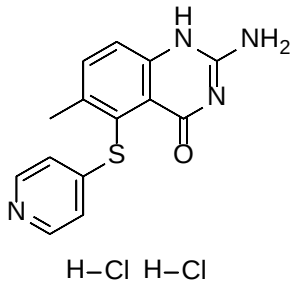
Product data sheet

MedKoo Cat#: 206596 Name: Nolatrexed HCl CAS#: 152946-68-4 (HCl salt) Chemical Formula: $C_{14}H_{14}Cl_2N_4OS$ Exact Mass: 356.0265 Molecular Weight: 357.25	
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:
Nolatrexed, also known as AG337, is a thymidylate synthase inhibitor with potential anticancer activity. A phase II study of nolatrexed in 2007 in advanced HCC patients demonstrated minimal activity and significant stomatitis. Hence, it does not warrant further study as a single agent for this disease.

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	15.0	42.0
Water	2.0	5.6

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.80 mL	14.00 mL	27.99 mL
5 mM	0.56 mL	2.80 mL	5.60 mL
10 mM	0.28 mL	1.40 mL	2.80 mL
50 mM	0.06 mL	0.28 mL	0.56 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. Webber S, Bartlett CA, Boritzki TJ, Hillard JA, Howland EF, Johnston AL, Kosa M, Margosiak SA, Morse CA, Shetty BV. AG337, a novel lipophilic thymidylate synthase inhibitor: in vitro and in vivo preclinical studies. Cancer Chemother Pharmacol. 1996;37(6):509-17. doi: 10.1007/s002800050422. PMID: 8612303.

In vivo study

1. Webber S, Bartlett CA, Boritzki TJ, Hillard JA, Howland EF, Johnston AL, Kosa M, Margosiak SA, Morse CA, Shetty BV. AG337, a novel lipophilic thymidylate synthase inhibitor: in vitro and in vivo preclinical studies. Cancer Chemother Pharmacol. 1996;37(6):509-17. doi: 10.1007/s002800050422. PMID: 8612303.

7. Bioactivity
Biological target: Nolatrexed dihydrochloride (AG 337) is a non-competitive lipophilic inhibitor of thymidylate synthase.

In vitro activity

AG337 inhibits purified recombinant human TS (thymidylate synthase) with a Ki of 11 nM, and displays non-competitive inhibition kinetics. It was further shown to inhibit cell growth in a panel of cell lines of murine and human origin, displaying an IC50 of between

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0.39 microM 6.6 microM. TS was suggested as the locus of action of AG337 by the ability of thymidine to antagonize cell growth inhibition and the direct demonstration of TS inhibition in whole cells using a tritium release assay. The demonstration, by flow cytometry, that AG337-treated L1210 cells were arrested in the S phase of the cell cycle was also consistent with a blockage of TS, as was the pattern of ribonucleotide and deoxyribonucleotide pool modulation in AG337-treated cells, which showed significant reduction in TTP levels.

Reference: Cancer Chemother Pharmacol. 1996;37(6):509-17. https://link.springer.com/article/10.1007%2Fs002800050422

In vivo activity

In vivo, AG337 was highly active against the thymidine kinase-deficient murine L5178Y/TK-lymphoma implanted either i.p. or i.m. following i.p. or oral delivery. Prolonged dosing periods of 5 or 10 days were required for activity, and efficacy was improved with twice-daily dose administration. Dose levels of 25 mg/kg delivered i.p. twice daily for 10 days, 50 mg/kg once daily for 10 days, or 100 mg/kg once daily for 5 days elicited 100% cures against the i.p. tumor. Doses required for activity against the i.m. tumor were higher (100 mg/kg i.p. twice daily for 5 or 10 days) but demonstrated the ability of AG337 to penetrate solid tissue barriers. Oral delivery required doses of > or = 150 mg/kg twice daily for periods of 5-10 days to produce 100% cure rates against both i.m. and i.p. implanted tumors.

Reference: Cancer Chemother Pharmacol. 1996;37(6):509-17. https://link.springer.com/article/10.1007%2Fs002800050422