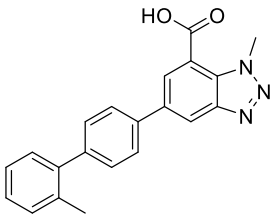
Product data sheet

MedKoo Cat#: 408160 Name: AG-636 CAS#: 1623416-31-8 Chemical Formula: $C_{21}H_{17}N_3O_2$ Exact Mass: 343.1321 Molecular Weight: 343.39	
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:
AG-636 is a potent, reversible, selective and orally active dihydroorotate dehydrogenase (DHODH) inhibitor with an IC50 of 17 nM. Differential AG-636 activity translated to the in vivo setting, with complete tumor regression observed in a lymphoma model. Dissection of the relationship between uridine availability and response to AG-636 revealed a divergent ability of lymphoma and solid tumor cell lines to survive and grow in the setting of depleted extracellular uridine and DHODH inhibition. Metabolic characterization paired with unbiased functional genomic and proteomic screens pointed to adaptive mechanisms to cope with nucleotide stress as contributing to response to AG-636.

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	31.25	91.00

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.91 mL	14.56 mL	29.12 mL
5 mM	0.58 mL	2.91 mL	5.82 mL
10 mM	0.29 mL	1.46 mL	2.91 mL
50 mM	0.06 mL	0.29 mL	0.58 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

TBD

In vivo study

McDonald G, Chubukov V, Coco J, Truskowski K, Narayanaswamy R, Choe S, Steadman M, Artin E, Padyana AK, Jin L, Ronseaux S, Locuson C, Fan ZP, Erdmann T, Mann A, Hayes S, Fletcher M, Nellore K, Rao SS, Subramanya H, Reddy KS, Panigrahi SK, Antony T, Gopinath S, Sui Z, Nagaraja N, Dang L, Lenz G, Hurov J, Biller SA, Murtie J, Marks KM, Ulanet DB. Selective Vulnerability to Pyrimidine Starvation in Hematologic Malignancies Revealed by AG-636, a Novel Clinical-Stage Inhibitor of Dihydroorotate Dehydrogenase. Mol Cancer Ther. 2020 Dec;19(12):2502-2515. doi: 10.1158/1535-7163.MCT-20-0550. Epub 2020 Oct 20. PMID: 33082276.

7. Bioactivity
Biological target:

Dihydroorotate dehydrogenase (DHODH)

Product data sheet

In vitro activity

TBD

In vivo activity

A chemical biology screen was performed, that revealed a strong enrichment in sensitivity to a novel dihydroorotate dehydrogenase (DHODH) inhibitor, AG-636, in cancer cell lines of hematologic versus solid tumor origin. Differential AG-636 activity translated to the in vivo setting, with complete tumor regression observed in a lymphoma model. Dissection of the relationship between uridine availability and response to AG-636 revealed a divergent ability of lymphoma and solid tumor cell lines to survive and grow in the setting of depleted extracellular uridine and DHODH inhibition. Metabolic characterization paired with unbiased functional genomic and proteomic screens pointed to adaptive mechanisms to cope with nucleotide stress as contributing to response to AG-636. These findings support targeting of DHODH in lymphoma and other hematologic malignancies and suggest combination strategies aimed at interfering with DNA-damage response pathways.

Reference: McDonald G, Chubukov V, Coco J, Truskowski K, Narayanaswamy R, Choe S, Steadman M, Artin E, Padyana AK, Jin L, Ronseaux S, Locuson C, Fan ZP, Erdmann T, Mann A, Hayes S, Fletcher M, Nellore K, Rao SS, Subramanya H, Reddy KS, Panigrahi SK, Antony T, Gopinath S, Sui Z, Nagaraja N, Dang L, Lenz G, Hurov J, Biller SA, Murtie J, Marks KM, Ulanet DB. Selective Vulnerability to Pyrimidine Starvation in Hematologic Malignancies Revealed by AG-636, a Novel Clinical-Stage Inhibitor of Dihydroorotate Dehydrogenase. Mol Cancer Ther. 2020 Dec;19(12):2502-2515. doi: 10.1158/1535-7163.MCT-20-0550. Epub 2020 Oct 20. PMID: 33082276.

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.