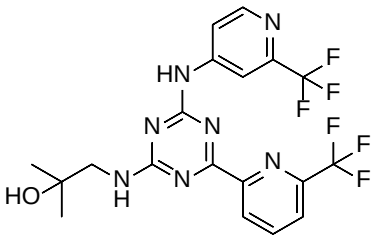
Product data sheet

MedKoo Cat#: 206438 Name: Enasidenib (AG-221) CAS#: 1446502-11-9 (free base) Chemical Formula: $C_{19}H_{17}F_6N_7O$ Exact Mass: 473.1399 Molecular Weight: 473.38	
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:
Enasidenib, also known as AG-221 and CC-90007, is a potent and selective IDH2 inhibitor with potential anticancer activity (IDH2 = Isocitrate dehydrogenase 2). The mutations of IDH2 present in certain cancer cells result in a new ability of the enzyme to catalyze the NAPH-dependent reduction of α-ketoglutarate to R(-)-2-hydroxyglutarate (2HG). The production of 2HG is believed to contribute to the formation and progression of cancer . The inhibition of mutant IDH2 and its neoactivity is therefore a potential therapeutic treatment for cancer.

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	91.67	193.65
Ethanol	100.0	211.25

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.11 mL	10.56 mL	21.12 mL
5 mM	0.42 mL	2.11 mL	4.22 mL
10 mM	0.21 mL	1.06 mL	2.11 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. Tong Z, Yerramilli U, Yao S, Young JD, Hoffmann M, Surapaneni S. In vitro inhibition of human nucleoside transporters and uptake of azacitidine by an isocitrate dehydrogenase-2 inhibitor enasidenib and its metabolite AGI-16903. Xenobiotica. 2019 Oct;49(10):1229-1236. doi: 10.1080/00498254.2018.1539783. Epub 2018 Nov 29. PMID: 30394160.

In vivo study

1. Yen K, Travins J, Wang F, David MD, Artin E, Straley K, Padyana A, Gross S, DeLaBarre B, Tobin E, Chen Y, Nagaraja R, Choe S, Jin L, Konteatis Z, Cianchetta G, Saunders JO, Salituro FG, Quivoron C, Opolon P, Bawa O, Saada V, Paci A, Broutin S, Bernard OA, de Botton S, Marteyn BS, Pilichowska M, Xu Y, Fang C, Jiang F, Wei W, Jin S, Silverman L, Liu W, Yang H, Dang L, Dorsch M, Penard-Lacronique V, Biller SA, Su SM. AG-221, a First-in-Class Therapy Targeting Acute Myeloid Leukemia Harboring Oncogenic IDH2 Mutations. Cancer Discov. 2017 May;7(5):478-493. doi: 10.1158/2159-8290.CD-16-1034. Epub 2017 Feb 13. PMID: 28193778.

7. Bioactivity

Product data sheet

Biological target: Enasidenib is an inhibitor of the IDH2 mutant enzymes with IC50s of 100 and 400 nM against IDH2R140Q and IDH2R172K, respectively.

In vitro activity

The inhibitory effects of enasidenib and its metabolite AGI-16903 on recombinant human nucleoside transporters (hNTs) in hNT-producing Xenopus laevis oocytes, and azacitidine uptake in a normal B-lymphoblast peripheral blood cell line (PBC) and acute myeloid leukemia (AML) cell lines were investigated. Enasidenib inhibited hENT1, hENT2, hENT3, and hENT4 in oocytes with IC50 values of 7, 63, 27, and 76 μM, respectively, but exhibited little inhibition of hCNT1-3. Azacitidine uptake was more than 2-fold higher in AML cells than in PBC. Enasidenib inhibited azacitidine uptake into OCI-AML2, TF-1 and PBC cells in a concentration-dependent manner with IC50 values of 0.27, 1.7, and 1.0 μM in sodium-containing transport medium, respectively. IC50 values shifted approximately 100-fold higher when human plasma was used as the incubation medium (27 μM in OCI-AML2, 162 μM in TF-1, and 129 μM in PBC), likely due to high human plasma protein binding of enasidenib (98.5% bound).

Reference: Xenobiotica. 2019 Oct;49(10):1229-1236.
https://www.tandfonline.com/doi/abs/10.1080/00498254.2018.1539783?journalCode=ixen20

In vivo activity

To determine if the in vivo differentiation effects of AG-221 were associated with a survival benefit, an aggressive human xenograft mouse model was established using early passage cells from a patient with AML harboring IDH2R140Q (AML-4; Supplementary Table S3). AG-221 treatment was well tolerated and, compared with vehicle, conferred a dose-dependent survival advantage that was statistically significant at doses of 15 and 45 mg/kg; there was also a statistically significant survival advantage with AG-221 45 mg/kg versus the vehicle ($P < 0.0001$; Fig. 4B). Four animals in the AG-221 45 mg/kg group remained on treatment after day 84, and all survived until study termination (day 130). This survival advantage was accompanied by reductions in 2HG levels and cell differentiation. As measured 8 hours after last dose (day 84), AG-221 exhibited a linear pharmacokinetic profile and effective inhibition of 2HG production in blood (89.7%, 91.9%, and 93.6%) and spleen (97.8%, 99.8, and 99.9%) at doses of 5, 15, and 45 mg/kg b.i.d., respectively. In BM, 2HG levels were below the limit of quantitation in all AG-221–treated animals except for two in the lowest dose group (both 93.3% inhibition; Supplementary Table S6).

Reference: Cancer Discov. 2017 May;7(5):478-493. https://cancerdiscovery.aacrjournals.org/content/7/5/478.long

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.