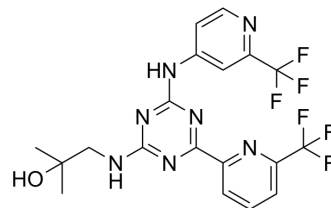


Enasidenib

Cat. No.:	HY-18690		
CAS No.:	1446502-11-9		
Molecular Formula:	C ₁₉ H ₁₇ F ₆ N ₇ O		
Molecular Weight:	473.38		
Target:	Isocitrate Dehydrogenase (IDH)		
Pathway:	Metabolic Enzyme/Protease		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro	DMSO : 50 mg/mL (105.62 mM; Need ultrasonic)					
		Solvent Concentration	Mass	1 mg	5 mg	10 mg
	Preparing Stock Solutions	1 mM		2.1125 mL	10.5623 mL	21.1247 mL
		5 mM		0.4225 mL	2.1125 mL	4.2249 mL
10 mM			0.2112 mL	1.0562 mL	2.1125 mL	
Please refer to the solubility information to select the appropriate solvent.						
In Vivo	<ol style="list-style-type: none"> Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: 2.08 mg/mL (4.39 mM); Suspended solution; Need ultrasonic and warming Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: ≥ 1.25 mg/mL (2.64 mM); Clear solution Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 1.25 mg/mL (2.64 mM); Clear solution 					

BIOLOGICAL ACTIVITY

Description	Enasidenib is an oral, potent, reversible, selective inhibitor of the IDH2 mutant enzymes, with IC ₅₀ s of 100 and 400 nM against IDH2 ^{R140Q} and IDH2 ^{R172K} , respectively.
IC₅₀ & Target	IC ₅₀ : 100 nM (IDH2 ^{R140Q}), 400 nM (IDH2 ^{R172K})[1]
In Vitro	Enasidenib (AG-221) reverses the effects of mutant IDH2 on DNA methylation in mutant stem/progenitor cells. Enasidenib induces differentiation and impairs self-renewal of IDH2-mutant leukemia cells, effects that are further enhanced by

simultaneous inhibition of Flt3^{ITD}. Enasidenib (AG-221) therapy induces differentiation of leukemic cells, with an increase in the CD11b⁺ population and a decrease in the c-Kit⁺ population in the peripheral blood at 2wks^[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Treatment with Enasidenib (AG-221) significantly improves survival in an IDH2-mutant acute myeloid leukemia (AML) primary xenograft mouse model^[1]. Enasidenib (AG-221), a mutant IDH2 inhibitor, remodels the epigenetic state of IDH2-mutant cells and induces alterations in self-renewal/differentiation in IDH2-mutant AML model in vivo. Enasidenib treatment (10mg/kg or 100mg/kg bid) leads to a reduction in 2-HG in vivo (96.7% below pre-treatment levels). Moreover, Enasidenib treatment restores megakaryocyte-erythroid progenitor (MEP) differentiation that is suppressed by mutant IDH2 expression (mean MEP% mean, 39% Veh vs 50% AG-221). Enasidenib therapy reverses the effects of mutant IDH2; a significant reduction is observed in DNA methylation, including 180 genes that have 20 or more hypomethylated differentially methylated cytosines (DMCs) following treatment. Enasidenib (100mg/kg bid) treatment of mice engrafted with Mx1-Cre IDH2^{R140Q}Flt3^{ITD} AML cells markedly reduces 2-hydroxyglutarate (2-HG) levels consistent with on target inhibition. Enasidenib inhibits mutant IDH2-mediated 2-HG production^[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Commun. 2022 Aug 15;13(1):4785.
- Cell Rep. 2022 Feb 15;38(7):110391.
- Sci Rep. 2018 Jun 21;8(1):9472.
- Sci Rep. 2017 Oct 6;7(1):12758.
- ACS Med Chem Lett. 2018 May 1;9(7):606-611.

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REFERENCES

[1]. Exploring the Pathway: IDH Mutations and Metabolic Dysregulation in Cancer Cells: A Novel Therapeutic Target. MAY 29, 2015

[2]. Alan H. Shih, et al. AG-221, a Small Molecule Mutant IDH2 Inhibitor, Remodels the Epigenetic State of IDH2-Mutant Cells and Induces Alterations in Self-Renewal/Differentiation in IDH2-Mutant AML Model in Vivo. Blood 2014 124:437.

Caution: Product has not been fully validated for medical applications. For research use only.

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