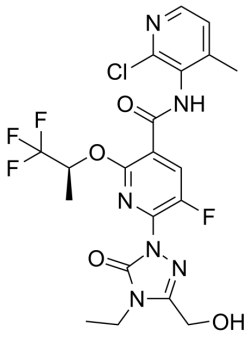
DHODH-IN-21

Cat. No.:	HY-149030
CAS No.:	2450341-39-4
Molecular Formula:	$C_{20}H_{19}ClF_4N_6O_4$
Molecular Weight:	518.85
Target:	Dihydroorotate Dehydrogenase
Pathway:	Metabolic Enzyme/Protease
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

DHODH-IN-21 (compound 19) is an orally active selective dihydroorotate dehydrogenase (DHODH) inhibitor with an IC_{50} value of 1.1 nM. DHODH-IN-21 has anticancer activity and can be used in studies of acute myeloid leukaemia (AML)[1].

IC_{50} & Target

Mouse DHODH	Rat DHODH	Dog DHODH	Monkey DHODH
140 nM (IC_{50})	1580 nM (IC_{50})	8.5 nM (IC_{50})	1.6 nM (IC_{50})

In Vitro

DHODH-IN-21 (compound 19) inhibits the proliferation of MOLM-13 and THP-1 cells with the IC_{50} values of 2.0 nM and 5.0 nM, respectively[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

DHODH-IN-21 (compound 19) (p.o., 10 or 20 mg/kg, everyday, 5 days) inhibits tumor growth in a dose-dependent manner but no effect on body weight in female NSG mice[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Human MOLM-13 AML xenograft model in female NSG mice[1]
Dosage:	10, 20 mg/kg
Administration:	Oral administration; everyday; 5 days
Result:	Inhibited tumor volume size by 44% and 60% at 10 mg/kg and 20 mg/kg respectively.

Animal Model:	Mouse, rat[1]
Dosage:	
Administration:	2 mg/kg i.v. or 10 mg/kg p.o.
Result:	The pharmacokinetic parameters of DHODH-IN-21 (compound 19)

Parameter	Mouse	Rat

CL (mL/min/kg)	11	32
V_{dss} (L/kg)	1.3	2.3
$t_{1/2}$(h)	2.3	2.0
C_{max} (ng/mL)	4047	1713
t_{max}(h)	0.42	1.7
$AUC_{0\rightarrow inf}$(h•ng/mL)	16,066	9214
F%	103	167

REFERENCES

[1]. Justin S Cisar, et al. N-Heterocyclic 3-Pyridyl Carboxamide Inhibitors of DHODH for the Treatment of Acute Myelogenous Leukemia. J Med Chem. 2022 Aug 4.

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