Mindeudesivir hydrobromide

Cat. No.: HY-145119AS

CAS No.: 2779498-79-0

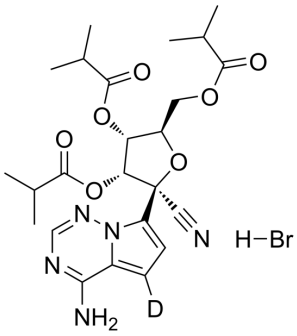
Molecular Formula: $C_{24}H_{31}DBrN_5O_7$

Molecular Weight: 583.45

Target: SARS-CoV; RSV; Influenza Virus

Pathway: Anti-infection

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (428.49 mM; Need ultrasonic)

Preparing Stock Solutions	Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
	1 mM	1.7139 mL	8.5697 mL	17.1394 mL
	5 mM	0.3428 mL	1.7139 mL	3.4279 mL
	10 mM	0.1714 mL	0.8570 mL	1.7139 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (3.57 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.57 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.57 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Mindeudesivir (JT001; VV116; GS-621763-d_1) hydrobromide is a deuterated version of Remdesivir (HY-104077), a highly orally active nucleoside antiviral against SARS-CoV-2 and respiratory syncytial virus (RSV). Mindeudesivir hydrobromide retains the antiviral activity of Remdesivir against COVID-19, and is the first domestically produced deuterium targeting the COVID-19[1][2].

IC_{50} & Target

SARS-CoV-2, RSV[1][2]

In Vitro

Stable heavy isotopes of hydrogen, carbon, and other elements have been incorporated into drug molecules, largely as tracers for quantitation during the drug development process. Deuteration has gained attention because of its potential to

affect the pharmacokinetic and metabolic profiles of drugs[1].
Potential advantages of deuterated compounds:
(1) Extend the half-life in vivo. Deuterated compounds may be able to prolong the pharmacokinetic characteristics of the compound, that is, prolong the half-life in vivo. This can improve compound safety, efficacy and tolerability, and increase ease of administration.
(2) Improve oral bioavailability. Deuterated compounds may reduce the degree of unwanted metabolism (first-pass metabolism) in the gut wall and liver, allowing a greater proportion of the unmetabolized drug to reach its target site of action. High bioavailability determines its activity at low doses and better tolerance.
(3) Improve metabolic characteristics. Deuterated compounds may reduce the formation of toxic or reactive metabolites and improve drug metabolism.
(4) Improve drug safety. Deuterated compounds may reduce or eliminate adverse side effects of pharmaceutical compounds and are safe.
(5) Preserve the therapeutic properties. Deuterated compounds are expected to retain similar biochemical potency and selectivity to hydrogen analogs in previous studies.

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

Cell Viability Assay

Cell Line:	A549 (infected with RSV)[1]
Concentration:	0-1000 μM
Incubation Time:	48 hours
Result:	Inhibited RSV replication in A549 cells with EC_{50} of 1.20 ± 0.32 μM, CC_{50} of 95.92 ± 9.27 μM and selectivity index (SI) of 80.

In Vivo

VV116 (25, 50 and 100 mg/kg; PO; b.i.d for 4 days) exhibits a stronger activity and decreases the virus titers below the detection limit at 50 mg/kg, also reduces lung injury after RSV infection[1].
VV116 (25, 50 and 100 mg/kg; PO; single dosage) exhibits favorable PK properties and good safety profile[1].
Pharmacokinetic Parameters of VV116 (JT001) in Balb/c mice[1].

	PO (25 mg/kg)	PO (50 mg/kg)	PO (100 mg/kg)
T_{max} (h)	0.42 ± 0.14	0.42 ± 0.14	0.42 ± 0.14
C_{max} (ng/mL)	5360 ± 560	11617 ± 3443	24017 ± 6521
AUC_{0-t} (ng/mL·h)	11461 ± 1013	24594 ± 1059	47799 ± 6545
$AUC_{0-\infty}$ (ng/mL·h)	11534 ± 992	24739 ± 1028	48014 ± 6696
$MRT_{0-\infty}$ (ng/mL·h)	2.25 ± 0.32	2.15 ± 0.26	2.28 ± 0.53
T_{max} (h)	2.30 ± 1.10	3.27 ± 1.92	4.25 ± 0.53

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

Animal Model:	Balb/c mice[1]
Dosage:	25, 50 and 100 mg/kg
Administration:	PO; single dosage (Pharmacokinetics Analysis)

Result:	Exhibited favorable PK properties and good safety profile.

Animal Model:	Balb/c mice (6-8 weeks; intranasally infected with 4 × 10^6 FFU of RSV)[1]
Dosage:	25, 50 and 100 mg/kg
Administration:	PO; b.i.d for 4 days
Result:	Exhibited a stronger activity and decreased the virus titers below the detection limit at 50 mg/kg, also reduced lung injury after RSV infection.

REFERENCES

[1]. Zhang R, et al. Oral remdesivir derivative VV116 is a potent inhibitor of respiratory syncytial virus with efficacy in mouse model. Signal Transduct Target Ther. 2022;7(1):123. Published 2022 Apr 16.

[2]. Qian HJ, et al. Safety, tolerability, and pharmacokinetics of VV116, an oral nucleoside analog against SARS-CoV-2, in Chinese healthy subjects [published online ahead of print, 2022 Mar 16]. Acta Pharmacol Sin. 2022;1-9.

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

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA