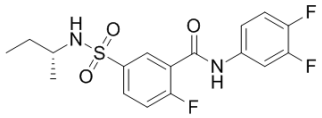
AB-423

Cat. No.:	HY-112142
CAS No.:	1572510-80-5
Molecular Formula:	$C_{17}H_{17}F_3N_2O_3S$
Molecular Weight:	386.39
Target:	HBV
Pathway:	Anti-infection
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 : ≥ 100 mg/mL (258.81 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.5881 mL	12.9403 mL	25.8806 mL
5 mM	0.5176 mL	2.5881 mL	5.1761 mL
10 mM	0.2588 mL	1.2940 mL	2.5881 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: ≥ 2.5 mg/mL (6.47 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.47 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AB-423 is an inhibitor of HBV capsid assembly, and potent inhibits HBV replication with EC_{50}/EC_{90} of 0.08-0.27 μM/0.33-1.32 μM in cells.

IC_{50} & Target

HBV capsid[1]

In Vitro

AB-423 is an inhibitor of HBV capsid assembly. AB-423 shows inhibitory effect on rcDNA production in AML12-HBV10 and HepDE19 cells with EC_{50}s of ~0.260 μM. AB-423 also suppresses cccDNA formation-dependent HBeAg production in the HepBHAe82 assay with an EC_{50} of 0.267 μM and inhibits HBV DNA levels in culture supernatants of HepG 2.2.15 cells with an EC_{50} of 0.134 μM. However, AB-423 has no cytotoxicity in any of the three cell lines[1].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	AB-423 (30 and 100 mg/kg, p.o. bid) blocks HBV replication in a mouse model of HBV. AB-423 (100 mg/kg, p.o. bid) with entecavir (ETV, 100 ng/mg, qd, p.o.) or 0.1 mg/kg dose of ARB-1467 potently inhibits serum HBV DNA in an HDI model of HBV in immunodeficient NOD-SCID mice[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	To test the compound combinations, HepBHAe82 (50,000 cells/well) are plated in 96-well tissue-culture treated microtiter plates in DMEM/F12 medium supplemented with 10% fetal bovine serum, 1% penicillin-streptomycin and tetracycline (1 μg/mL), and incubated in a humidified incubator at 37°C and 5% CO_2 overnight. On the next day, the cells are switched to fresh medium and treated with inhibitor A and inhibitor B, at concentration range in the vicinity of their respective EC_{50} values. The inhibitors are either diluted in 100% DMSO (ETV, TDF and AB-423) or growth medium (ARB-1467 and ARB-1740) and the final DMSO concentration in the assay is ≤0.5%. The two inhibitors are tested both singly as well as in combinations determine their effects on inhibition of rcDNA production. The final DMSO concentration in the assay is 0.5%. The plates are incubated for 9 days in a humidified incubator at 37°C and 5% CO_2. Following a 9 day-incubation, medium is removed, and cells are subjected to RNA extraction to measure the cccDNA-dependent precore mRNA level[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] Prior to start of treatment, 10 micrograms of the plasmid pHBV1.3 is administered to NOD.CB17-Prkdcscid/J mice via hydrodynamic injection (HDI; rapid high volume injection into the tail vein; n = 6 to 8 animals per group). This plasmid carries a 1.3-fold overlength copy of a HBV genotype D genome which, when expressed, generates hepatitis B viral particles and other HBV products. AB-423 is administered via oral gavage at 30 or 100 mg/kg twice-daily for 7 consecutive days, starting on Day 0. Entecavir (ETV) at 100 ng/kg once-daily for 7 consecutive days, starting on Day 0. ARB-1467 is administered as a single intravenous bolus tail vein injection at 0.1 mg/kg on Day 0. Blood is collected on Days 0 (pre-dose), 4 and 7 for HBV biomarker analysis. Serum HBV DNA concentration in mice is measured from total extracted DNA using a quantitative PCR assay using primer/probe sequences[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Virus Res. 2019 Oct 2;271:197677.

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REFERENCES

[1]. Mani N, et al. Preclinical profile of AB-423, an inhibitor of Hepatitis B virus pgRNA encapsidation. Antimicrob Agents Chemother. 2018 Mar 19.

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

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