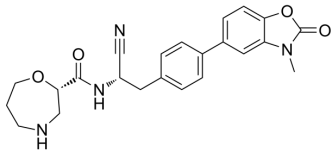
Brensocatib

Cat. No.:	HY-101056
CAS No.:	1802148-05-5
Molecular Formula:	$C_{23}H_{24}N_4O_4$
Molecular Weight:	420
Target:	Dipeptidyl Peptidase
Pathway:	Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (238.10 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3810 mL	11.9048 mL	23.8095 mL
	5 mM	0.4762 mL	2.3810 mL	4.7619 mL
	10 mM	0.2381 mL	1.1905 mL	2.3810 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 (5.95 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.95 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Brensocatib (AZD7986) is an oral dipeptidyl peptidase 1 (DPP1) inhibitor with pIC_{50}s of 6.85, 7.6, 7.7, 7.8, and 7.8 in human, mouse, rat, dog and rabbit, respectively[1].

IC_{50} & Target

DPP-1

In Vitro

Results from cell assay show that Brensocatib (AZD7986) is a Dipeptidyl peptidase 1 (DPP1) inhibitor with pIC_{50}s of 6.85, 7.6, 7.7, 7.8, and 7.8 in human, mouse, rat, dog and rabbit, respectively. Brensocatib is stable in the propionaldehyde reactivity assay, with a half-life over 50 h. After differentiation in the presence of Brensocatib (38 pM to 10 μM), concentration-dependent decreases in cell lysate enzyme activity are observed for DPP1, as well as for all of the three NSPs, NE, Pr3, and CatG. Brensocatib inhibits activation of all three NSPs in a concentration dependent manner, with pIC_{50} values of around 7

	for all three NSPs. The reduction of the activities is almost complete, with NE, Pr3, and CatG activities reduced to 4 to 10% of control at 10 μM Brensocatib[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Brensocatib (AZD7986) shows good stability in plasma, with a half life of >10 h. Brensocatib inhibits activation of NE and Pr3, but not CatG, in bone marrow cell lysates in a dose dependent manner in vivo[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Cellular potency is studied using the DPP1-expressing monocytic U937 cell line. Briefly, cells grown in RPMI are plated on 384-well polypropylene v-bottom plates at a density of 5×10^5 cells/mL per well. Added to this is 10 μL of Brensocatib at 37°C for 60 min, followed by 350 μM Gly-Phe-AFC. The well fluorescence is read using a multilabel plate reader. Data are analyzed to calculate pIC_{50} values[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Rats are used for the in vivo study. Naive rats are dosed orally twice daily with Brensocatib at 0.2, 2, and 20 mg/kg/day for 8 days. Attermination, bone marrow is taken by femural aspiration for neutrophil serine proteases (NSPs) activity analysis using commercial synthetic peptide substrates[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cancer Cell. 2021 Mar 8;39(3):423-437.e7.
- Biochem Pharmacol. 2019 Jun;164:349-367.

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REFERENCES

[1]. Doyle K, et al. Discovery of Second Generation Reversible Covalent DPP1 Inhibitors Leading to an Oxazepane Amidoacetonitrile Based Clinical Candidate (AZD7986). J Med Chem. 2016 Oct 27;59(20):9457-9472.

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