Cenicriviroc

Cat. No.: HY-14882

CAS No.: 497223-25-3

Molecular Formula: $C_{41}H_{52}N_4O_4S$

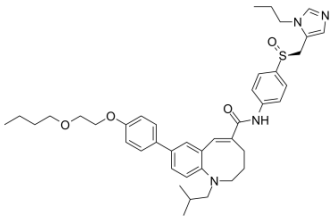
Molecular Weight: 696.94

Target: CCR; HIV

Pathway: GPCR/G Protein; Immunology/Inflammation; 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 : 50 mg/mL (71.74 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.4348 mL	7.1742 mL	14.3484 mL
5 mM	0.2870 mL	1.4348 mL	2.8697 mL
10 mM	0.1435 mL	0.7174 mL	1.4348 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 (2.98 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (2.98 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Cenicriviroc (TAK-652) is an orally active, dual CCR2/CCR5 antagonist, also inhibits both HIV-1 and HIV-2, and displays potent anti-inflammatory and antiinfective activity[1].

IC_{50} & Target

CCR5	CCR2	R5 HIV-1	R5 HIV-2
0.29 nM (IC_{50})	5.9 nM (IC_{50})	0.024-0.08 nM (IC_{50}, in PBMCs)	0.03-0.98 nM (IC_{50}, in PBMCs)

In Vitro

Cenicriviroc prevents human immunodeficiency virus type 1 (HIV-1) from cellular entry[2]. Regarding the 4 R5 HIV-2 clinical isolates tested, effective concentration 50% EC_{50} for cenicriviroc are 0.03, 0.33, 0.45 and 0.98 nM. The dual-tropic and the X4-

	tropic HIV-2 strains are resistant to cenicriviroc with EC_{50} at >1000 nM, and MPI at 33% and 4%, respectively[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Cenicriviroc (≥20 mg/kg/day) significantly reduces monocyte/macrophage recruitment in vivo. At these doses, cenicriviroc shows antifibrotic effects, with significant reductions in collagen deposition, and collagen type 1 protein and mRNA expression across the three animal models of fibrosis. In the NASH model, cenicriviroc significantly reduces the non-alcoholic fatty liver disease activity score. Cenicriviroc treatment has no notable effect on body or liver/kidney weight[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Male C57BL/6 mice (n=44; 8-10 weeks of age) are allocated to receive treatments via oral gavage (PO) on Days 1-5 in the following groups: non-disease control, vehicle control twice daily (BID), Cenicriviroc 5 mg/kg/day (Cenicriviroc5) BID, Cenicriviroc 20 mg/kg/day (Cenicriviroc20) BID, Cenicriviroc 100 mg/kg/day (Cenicriviroc100) BID, Cenicriviroc20 QD, and positive control (corticosteroid known to reduce inflammation in a variety of animal models) 1 mg/kg QD. On Day 4, peritonitis is induced via IP injection of TG 3.85% (1 mL/animal) 2 hours post-dose in all groups except non-disease controls. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Biomaterials. 2020, 120392.
- Cells. 2020 Apr 14;9(4). pii: E964.
- Antiviral Res. 2020 Jul 30;104902.

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REFERENCES

[1]. Lefebvre E, et al. Antifibrotic Effects of the Dual CCR2/CCR5 Antagonist Cenicriviroc in Animal Models of Liver and Kidney Fibrosis. PLoS One. 2016 Jun 27;11(6):e0158156

[2]. Kuwata T, et al. Incompatible Natures of the HIV-1 Envelope in Resistance to the CCR5 Antagonist Cenicriviroc and to Neutralizing Antibodies. Antimicrob Agents Chemother. 2015 Nov 2;60(1):437-5

[3]. Visseaux B, et al. Cenicriviroc, a Novel CCR5 (R5) and CCR2 Antagonist, Shows In Vitro Activity against R5 Tropic HIV-2 Clinical Isolates. PLoS One. 2015 Aug 6;10(8):e0134904

[4]. Lalezari J, et al. Safety, efficacy, and pharmacokinetics of TBR-652, a CCR5/CCR2 antagonist, in HIV-1-infected, treatment-experienced, CCR5 antagonist-naive subjects. J Acquir Immune Defic Syndr. 2011 Jun 1;57(2):118-25.

[5]. Baba M, et al. TAK-652 inhibits CCR5-mediated human immunodeficiency virus type 1 infection in vitro and has favorable pharmacokinetics in humans. Antimicrob Agents Chemother. 2005 Nov;49(11):4584-91.

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

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