Cenicriviroc Mesylate

Cat. No.: HY-14882A

CAS No.: 497223-28-6

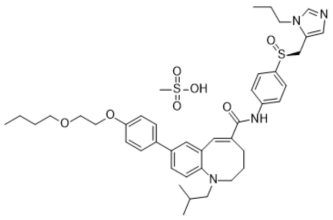
Molecular Formula: $C_{42}H_{56}N_4O_7S_2$

Molecular Weight: 793.05

Target: CCR; HIV

Pathway: GPCR/G Protein; Immunology/Inflammation; 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 : 100 mg/mL (126.10 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.2610 mL	6.3048 mL	12.6095 mL
	5 mM	0.2522 mL	1.2610 mL	2.5219 mL
	10 mM	0.1261 mL	0.6305 mL	1.2610 mL

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

In Vivo

1. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: 2.5 mg/mL (3.15 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (2.62 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (2.62 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Cenicriviroc Mesylate (TAK-652 Mesylate) is a dual CCR2/CCR5 antagonist, also inhibits both HIV-1 and HIV-2, and displays potent anti-inflammatory and antiinfective activity.

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

In Vitro

Migration of mouse monocytes in response to carbon tetrachloride (CCL2) is reduced following pre-treatment with Cenicriviroc Mesylate (CVC) at a concentration of 1 μM. Compare to untreated and unstimulated cells, the average fold

	change in migrating cells (±SD) is 0.8±0.2 (p>0.05) and 0.7±0.4 (p>0.05) for CCL2-stimulated cells treated with Cenicriviroc Mesylate and unstimulated cells treated with Cenicriviroc Mesylate, respectively[1]. Phenotypic susceptibility testing shows, for the four R5-tropic HIV-2 isolates, a median EC_{50} for Cenicriviroc Mesylate of 0.39 nM (0.03, 0.33, 0.45 and 0.98 nM). The dual-tropic and the X4-tropic HIV-2 strains are resistant to Cenicriviroc Mesylate with EC_{50} at >1000 nM, and Maximum percentages of inhibition (MPI) at 33% and 4%, respectively[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Cenicriviroc Mesylate (CVC) treatment leads to dose-related decrease in monocyte/macrophage recruitment, and achieving statistical significance at doses ≥20 mg/kg/day (p<0.05). Compare to the vehicle-control group, peritoneal lavage monocyte/macrophage counts are decreased by: 5.7%, 45.2%, 76.5% and 26.0% for Cenicriviroc Mesylate 5 twice daily (BID), Cenicriviroc Mesylate20 twice daily (BID), Cenicriviroc Mesylate100 BID, Cenicriviroc Mesylate 20 once-daily (QD), respectively. Exposure to Cenicriviroc Mesylate is dose-related and correlated with the decrease in monocyte/macrophage recruitment, with Cenicriviroc Mesylate appearing to be more effective when given BID versus QD, in line with the higher plasma concentrations achieved with BID dosing and the known short half-life in mice (~2 hours)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Mouse monocyte migration in response to Cenicriviroc Mesylate (CVC) treatment is assessed ex vivo in triplicate. Thioglycollate (TG) is injected intraperitoneally into male C57BL/6 mice (n=3; 8 to 10 weeks of age) and activated macrophages are collected 48 hours later by peritoneal lavage. Cells are incubated for 2 hours in the presence of 1 μM Cenicriviroc Mesylate. Cells are harvested from the lower compartment and analyzed by flow cytometry to enumerate F4/80 $^{+}$CD11b^{+} macrophages. Results are analyzed using FlowJo software[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Male C57BL/6 mice (n=44; 8 to 10 weeks of age) are allocated to receive treatments via oral gavage (PO) on Days 1 to 5 in the following groups: non-disease control, vehicle control twice daily (BID), Cenicriviroc Mesylate 5 mg/kg/day (CVC5) BID, Cenicriviroc Mesylate 20 mg/kg/day (CVC20) BID, Cenicriviroc Mesylate 100 mg/kg/day (CVC100) BID, Cenicriviroc Mesylate 20 mg/kg once-daily (QD). On Day 4, peritonitis is induced via IP injection of thioglycollate (TG) 3.85% (1 mL/animal) 2 hours post-dose in all groups except non-disease controls[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Biomaterials. 2021 Jan;265:120392.
- Cells. 2020 Apr 14;9(4):964.
- Antiviral Res. 2020 Oct;182:104902.

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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]. 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.

[3]. 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.

[4]. 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.

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