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产品名称：Cenicriviroc
产品别名：TAK-652; TBR-652

生物活性：

Description	Cenicriviroc is an orally active, dual CCR2/CCR5 antagonist, also inhibits both HIV-1 and HIV-2, and displays potent anti-inflammatory and antiinfective activity.			
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% EC50 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 EC50 at >1000 nM, and MPI at 33% and 4%, respectively[3].			
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].			

Solvent&Solubility

In Vitro:

DMSO : ≥ 125 mg/mL (179.36 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
Preparing Stock Solutions	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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.08 mg/mL (2.98 mM); Clear solution

此方案可获得 ≥ 2.08 mg/mL (2.98 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 20.8 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

	2.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.08 mg/mL (2.98 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (2.98 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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.

实验参考：

Animal Administration	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. [1]
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.