



上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话: 021-61312973 传真: 021-55068248
网址: www.shyuanye.com
邮箱: shyysw@sina.com

产品名称: **Lersivirine**
产品别名: **UK-453061**

生物活性:

Description

Lersivirine(UK-453061) is a next-generation non-nucleoside reverse transcriptase inhibitor (NNRTI, IC50=119 nM) with a unique resistance profile that exhibits potent antiretroviral activity against wild-type human immunodeficiency virus and clinically relevant NNRTI-resistant strains. IC50 value: 0.119 uM [1]
Target: NNRTI UK-453061(Compound 5) demonstrated excellent activity against large panels of wild type and drug-resistant HIV consistent with the encouraging profile demonstrated against the isolated RT enzymes. Compound 5 can be readily prepared in multi-gram quantities by virtue of the efficient and concise synthetic route. The compound also has good aqueous solubility and formulation characteristics which enable further in vivo evaluation. Clinical trials evaluating the potential of 5 (UK-453,061, lersivirine) to treat HIV infection are proceeding and further progress will be reported in due course [1]. At clinically relevant lersivirine doses (500-1,000 mg total daily dose), the mean plasma exposure of midazolam was reduced in a dose-dependent manner by 20-36 %. Co-administration of lersivirine 1,000 mg QD with OCs had minor PK effects, increasing ethinylestradiol exposure by 10 % and reducing levonorgestrel exposure by 13 % [2]. Mated Crl:CD1(ICR) mice were administered 0, 150, 350, and 500 mg/kg lersivirine once daily by oral gavage on gestation days 6 to 17, followed by cesarean section on gestation day 18. The first 2 days of dosing for the high-dose group were done at 250 mg/kg to allow induction of hepatic metabolizing enzymes, after which the dose was increased to 500 mg/kg/day [3].

In Vitro:

DMSO : 50 mg/mL (161.11 mM; Need ultrasonic)

H₂O : < 0.1 mg/mL (insoluble)

Preparing	Solvent	Mass	1 mg	5 mg	10 mg
	Concentration				
		1 mM	3.2222 mL	16.1108 mL	32.2217 mL
Stock Solutions	5 mM	0.6444 mL	3.2222 mL	6.4443 mL	
	10 mM	0.3222 mL	1.6111 mL	3.2222 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: ≥ 3 mg/mL (9.67 mM); Clear solution

此方案可获得 ≥ 3 mg/mL (9.67 mM, 饱和度未知) 的澄清溶液。

Solvent&Solubility



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	以 1 mL 工作液为例, 取 100 μ L 30.0 mg/mL 的澄清 DMSO 储备液加到 400 μ L PEG300 中, 混合均匀向上述体系中加入 50 μ L Tween-80, 混合均匀; 然后继续加入 450 μ L 生理盐水定容至 1 mL。
References	[1]. Mowbray CE, et al. Pyrazole NNRTIs 4: selection of UK-453,061 (lorsivirine) as a development candidate. Bioorg Med Chem Lett. 2009 Oct 15;19(20):5857-60. [2]. Davis J, et al. The effect of lorsivirine, a next-generation NNRTI, on the pharmacokinetics of midazolam and oral contraceptives in healthy subjects. Eur J Clin Pharmacol. 2012 Nov;68(11):1567-72. [3]. Cappon GD, et al. Developmental toxicity study of lorsivirine in mice. Birth Defects Res B Dev Reprod Toxicol. 2012 Jun;95(3):225-30.



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