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产品名称：MK-5172 (hydrate)
产品别名：Grazoprevir hydrate

生物活性：

Description	Grazoprevir hydrate (MK-5172 hydrate) is a selective inhibitor of Hepatitis C virus NS3/4a protease with broad activity across genotypes and resistant variants, with Kis of 0.01 nM (gt1b), 0.01 nM (gt1a), 0.08 nM (gt2a), 0.15 nM (gt2b), 0.90 nM (gt3a), respectively.
IC_{50} & Target	Ki: 0.01±<0.01 nM (gt1b), 0.01±0.01 nM (gt1a), 0.08±0.02 nM (gt2a), 0.15±0.06 nM (gt2b), 0.90±0.2 nM (gt3a)[1]
In Vitro	In biochemical assays, Grazoprevir (MK-5172) is effective against a panel of major genotypes and variants engineered with common resistant mutations, with K_i of 0.01±<0.01 nM (gt1b), 0.01±0.01 nM (gt1a), 0.08±0.02 nM (gt2a), 0.15±0.06 nM (gt2b), 0.90±0.2 nM (gt3a), 0.07±0.01 nM ($gt1b^{R155K}$), 0.14±0.03 nM ($gt1b^{D168V}$), 0.30±0.04 nM ($gt1b^{D168Y}$), 5.3±0.9 nM ($gt1b^{A156T}$), and 12±2 nM ($gt1b^{A156V}$), respectively. In the replicon assay, Grazoprevir demonstrates subnanomolar to low-nanomolar EC_{50}s against genotypes 1a, 1b, and 2a, with EC_{50}s of 0.5±0.1 nM, 2±1 nM, and 2±1 nM for $gt1b^{con1}$, gt1a, and gt2a, respectively. Grazoprevir is potent against a panel of HCV replication mutants NS5A (Y93H) (EC_{50}=0.7±0.3 nM), NS5B nucleosides (S282T) (EC_{50}=0.3±0.1 nM), and NS5B (C316Y) (EC_{50}=0.4±0.2)[1]. Grazoprevir (MK-5172) maintains the excellent potency against the gt 3a enzyme as well as a broad panel of mutant enzymes, has excellent potency in the replicon system [gt1b IC_{50}(50% NHS)=7.4 nM; gt1a IC_{50}(40% NHS)=7 nM], and shows excellent rat liver exposure[2].
In Vivo	Grazoprevir (MK-5172) demonstrates efficacy in vivo against chronic-HCV-infected chimpanzees[1]. When dosed to dogs, Grazoprevir (MK-5172) shows low clearance of 5 mL/min/kg and a 3 h half-life after iv dosing and has good plasma exposure (AUC=0.4 μM h) after a 1 mg/kg oral dose. Dog liver biopsy studies showed that the liver concentration of Grazoprevir after the 1 mg/kg oral dose is 1.4 μM at the 24 h time point. Similar to its behavior in rats, Grazoprevir demonstrates effective partitioning into liver tissue and maintains high liver concentration, relative to potency, 24 h after oral dosing in dogs[2].

In Vitro:

DMSO : 50 mg/mL (63.70 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	**1 mg**	**5 mg**	**10 mg**
	1 mM	1.2740 mL	6.3701 mL	12.7402 mL
	5 mM	0.2548 mL	1.2740 mL	2.5480 mL
	10 mM	0.1274 mL	0.6370 mL	1.2740 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：

Solvent&Solubility	——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: ≥ 2.5 mg/mL (3.19 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (3.19 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 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: ≥ 2.5 mg/mL (3.19 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (3.19 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 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Steven Harper , John A. McCauley , Michael T. Discovery of MK-5172, a Macrocyclic Hepatitis C Virus NS3/4a Protease Inhibitor. ACS Med. Chem. Lett., 2012, 3 (4), pp 332-336 [2]. Summa V, Ludmerer SW, McCauley JA, MK-5172, a selective inhibitor of hepatitis C virus NS3/4a protease with broad activity across genotypes and resistant variants. Antimicrob Agents Chemother. 2012 Aug;56(8):4161-7.