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产品名称：BENZIMIDAVIR 苯并咪唑核苷
产品别名：Maribavir ；马立巴韦；1263W94; BW1263W94; GW257406X

生物活性：

Description	Maribavir is a potent inhibitor of histone phosphorylation catalyzed by wild-type pUL97 in vitro, with an IC_{50} of 3 nM. Maribavir has potent antiviral activity against HCMV and Epstein-Barr virus (EBV).
IC_{50} & Target	HCMV[1]
In Vitro	Maribavir is a potent inhibitor of the autophosporylation of the wild type and all the major Ganciclovir (GCV) resistant UL97 mutants analysed with a mean IC_{50} of 35 nM. The M460I mutation results in hypersensitivity to Maribavir with an IC_{50} of 4.8 nM. A Maribavir resistant mutant of UL97 (L397R) is functionally compromised as both a Ganciclovir kinase and a protein kinase (~ 10% of wild type levels). Enzyme kinetic experiments demonstrate that Maribavir is a competitive inhibitor of ATP with a K_i of 10 nM[1]. Maribavir (1263W94) inhibits viral replication in a dose-dependent manner, with IC_{50} of 0.12±0.01 μM as measured by a multicycle DNA hybridization assay. The pUL97 protein kinase is strongly inhibited by Maribavir, with 50% inhibition occurring at 3 nM[2].
Solvent&Solubility	***In Vitro:*** **DMSO： ≥ 51 mg/mL (135.55 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.6579 mL	13.2894 mL	26.5788 mL
	5 mM	0.5316 mL	2.6579 mL	5.3158 mL
	10 mM	0.2658 mL	1.3289 mL	2.6579 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: ≥ 2.5 mg/mL (6.64 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (6.64 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% (20% SBE-β-CD in saline)

Solubility: ≥ 2.5 mg/mL (6.64 mM); Clear solution

	此方案可获得 ≥ 2.5 mg/mL (6.64 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 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (6.64 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.64 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]. Shannon-Lowe CD, et al. The effects of Maribavir on the autophosphorylation of ganciclovir resistant mutants of the cytomegalovirus UL97 protein. Herpesviridae. 2010 Dec 7;1(1):4. [2]. Biron KK, et al. Potent and selective inhibition of human cytomegalovirus replication by 1263W94, a benzimidazole L-riboside with a unique mode of action. Antimicrob Agents Chemother. 2002 Aug;46(8):2365-72.
实验参考：	
Cell Assay	For these studies MRC-5 cells are seeded in 24-well plates at ~5×10^4 cells/well and grown for 3 days in MEM 8-1-1 to confluence (~1.1×10^5 cells/well). The cells are infected with AD169 in MEM 2-1-1 at an MOI ranging from 1 to 3 and incubated at 37°C for 90 min to allow viral adsorption. The unadsorbed virus is removed and replaced with 1 mL of MEM 2-1-1. To test the effect of compounds on viral DNA synthesis or maturation, Maribavir, BDCRB, or GCV is added to the medium at the concentrations indicated for each experiment[2].
Kinase Assay	Enzyme kinetic analysis is performed on the purified wild type and mutant UL97 protein species using increasing concentrations of ATP (2 μM to 20 μM). The amount of incorporated radiolabelled phosphate is plotted against the concentration of ATP in a Lineweaver Burke plot to determine the K_m for ATP for each UL97 species. The effect of Maribavir upon the rate of radiolabelled phosphate incorporation by wild type or mutant UL97 is determined by protein kinase assays at a fixed concentration of Maribavir (0.5 μM) as above, or with increasing concentrations of Maribavir (0.01 μM to 5.0 μM) to determine the IC_{50} of Maribavir for each UL97 species. In order to determine the nature of the inhibition mediated by Maribavir, plots of 1/v vs 1/ATP with increasing concentrations of Maribavir are constructed. Competitive inhibition is evident if the family of lines cconverged on the y-axis at 1/Vmax. The change in slope caused by the addition of Maribavir is used to calculate the K_i[1].
References	[1]. Shannon-Lowe CD, et al. The effects of Maribavir on the autophosphorylation of ganciclovir resistant mutants of the cytomegalovirus UL97 protein. Herpesviridae. 2010 Dec 7;1(1):4. [2]. Biron KK, et al. Potent and selective inhibition of human cytomegalovirus replication by 1263W94, a benzimidazole L-riboside with a unique mode of action. Antimicrob Agents Chemother. 2002 Aug;46(8):2365-72.