产品名称：Nepicastat (SYN-117) HCl
产品别名：内匹司他盐酸盐 ；Nepicastat hydrochloride

生物活性：

Description	Nepicastat hydrochloride (SYN-117 hydrochloride) is a selective, potent, and orally active inhibitor of dopamine-beta-hydroxylase. Nepicastat hydrochloride produces concentration-dependent inhibition of bovine (IC50=8.5 nM) and human (IC50=9 nM) dopamine-beta-hydroxylase. Nepicastat hydrochloride can cross the blood-brain barrier (BBB)[1][2][3].
IC_{50} & Target	IC50: 8.5 nM (bovine dopamine-beta-hydroxylase), 9 nM (human dopamine-beta-hydroxylase)[2]
In Vivo	Nepicastat hydrochloride (SYN-117 hydrochloride) (3-100 mg/kg; p.o.; three consecutive times, 12 hours apart times) produces dose-dependent decreases in noradrenaline content, increases in dopamine content and increases in dopamine/noradrenaline ratio in the artery (mesenteric or renal), left ventricle[3].

Animal Model:	15-16 weeks male spontaneously hypertensive rats (SHRs)[3]
Dosage:	3, 10, 30, 100 mg/kg
Administration:	Oral administration; three consecutive times, 12 hours apart
Result:	Produced dose-dependent decreases in noradrenaline content, increases in dopamine content and increases in dopamine/noradrenaline ratio in the artery (mesenteric or renal), left ventricle and cerebral cortex.

Solvent&Solubility

In Vitro:

DMSO : 6 mg/mL (**18.08 mM;** Need ultrasonic)

H_2O : 2 mg/mL (**6.03 mM;** Need ultrasonic and warming)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.0138 mL	15.0689 mL	30.1377 mL
5 mM	0.6028 mL	3.0138 mL	6.0275 mL
10 mM	0.3014 mL	1.5069 mL	3.0138 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: ≥ 0.6 mg/mL (1.81 mM); Clear solution

此方案可获得 ≥ 0.6 mg/mL (1.81 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 6.0 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: ≥ 0.6 mg/mL (1.81 mM); Clear solution 此方案可获得 ≥ 0.6 mg/mL (1.81 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 6.0 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: ≥ 0.6 mg/mL (1.81 mM); Clear solution 此方案可获得 ≥ 0.6 mg/mL (1.81 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 6.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Beliaev A, et al. Synthesis and biological evaluation of novel, peripherally selective chromanyl imidazolethione-based inhibitors of dopamine beta-hydroxylase.J Med Chem. 2006 Feb 9;49(3):1191-7. [2]. Stanley WC, et al. Cardiovascular effects of nepicastat (RS-25560-197), a novel dopamine beta-hydroxylase inhibitor. J Cardiovasc Pharmacol. 1998 Jun;31(6):963-70. [3]. Stanley WC, et al. Catecholamine modulatory effects of nepicastat (RS-25560-197), a novel, potent and selective inhibitor of dopamine-beta-hydroxylase. Br J Pharmacol. 1997 Aug;121(8):1803-9. [4]. Sabbah HN, et al. Effects of dopamine beta-hydroxylase inhibition with nepicastat on the progression of left ventricular dysfunction and remodeling in dogs with chronic heart failure.