产品名称：Sitaxentan sodium
产品别名：司他生坦钠

生物活性：

Description	Sitaxsentan sodium (IPI 1040 sodium; TBC11251 sodium) is an orally active, highly selective antagonist of endothelin A receptors.
In Vitro	Sitaxsentan and Bosentan attenuate NTCP transport at higher concentrations, and inhibit human hepatic transporters, which provides a potential mechanism for the increased hepatotoxicity observed for these agents in the clinical setting. Only sitaxsentan decreased OATP transport (52%)[1]. Sitaxsentan and sitaxsentan combined with sildenafil completely prevent the increased expressions of endothelin-1 and of the ETB receptor. Sitaxsentan alone partially restores the expressions of BMPR-1A and BMPR-2. The combination of sildenafil and sitaxsentan further restores the expressions of BMPR-1A and BMPR-2, which remaines, however, decreased compared with controls[3].
In Vivo	Sitaxsentan (5 mg/kg infused iv 10 min prior to onset of hypoxia) completely blocks hypoxia-induced vasoconstriction and this group does not differ from air controls. Oral administration of sitaxsentan, significantly attenuates the increase in MPAP, while the administration of sitaxsentan to rats exposed to normal oxygen levels is without effect on MPAP[2]. Sitaxsentan alone limits shunt-induced increase in MT. Sitaxsentan combined with sildenafil more effectively prevents this remodeling, which, however, tends to remain increased compared with controls[3].
Solvent&Solubility	***In Vitro:*** **DMSO : 100 mg/mL (209.69 mM;** Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0969 mL	10.4846 mL	20.9692 mL
	5 mM	0.4194 mL	2.0969 mL	4.1938 mL
	10 mM	0.2097 mL	1.0485 mL	2.0969 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 (5.24 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.24 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 (5.24 mM); Clear solution

	此方案可获得 ≥ 2.5 mg/mL (5.24 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。
References	[1]. Hartman JC, et al. Evaluation of the endothelin receptor antagonists ambrisentan, darusentan, bosentan, and sitaxsentan as substrates and inhibitors of hepatobiliary transporters in sandwich-cultured human hepatocytes. Can J Physiol Pharmacol. 2010 Jun;88 [2]. Tilton RG, et al. Attenuation of pulmonary vascular hypertension and cardiac hypertrophy with sitaxsentan sodium, an orally active ET(A) receptor antagonist. Pulm Pharmacol Ther. 2000;13(2):87-97. [3]. Rondelet B, et al. Sildenafil added to sitaxsentan in overcirculation-induced pulmonary arterial hypertension. Am J Physiol Heart Circ Physiol. 2010 Oct;299(4):H1118-23. Epub 2010 Aug 6.

实验参考：

Animal Administration	After an initial 2-week period of hypoxic exposure (10% O_2) sitaxsentan (15 or 30 mg/kg body weight per day in the drinking water) is administered for 4 weeks during continuous exposure to hypoxia. At the conclusion of the 4 week period of hypoxia, femoral and pulmonary arterial cannulation and measurement of MPAP, MSAP, and HR are performed. [2]
References	[1]. Hartman JC, et al. Evaluation of the endothelin receptor antagonists ambrisentan, darusentan, bosentan, and sitaxsentan as substrates and inhibitors of hepatobiliary transporters in sandwich-cultured human hepatocytes. Can J Physiol Pharmacol. 2010 Jun;88 [2]. Tilton RG, et al. Attenuation of pulmonary vascular hypertension and cardiac hypertrophy with sitaxsentan sodium, an orally active ET(A) receptor antagonist. Pulm Pharmacol Ther. 2000;13(2):87-97. [3]. Rondelet B, et al. Sildenafil added to sitaxsentan in overcirculation-induced pulmonary arterial hypertension. Am J Physiol Heart Circ Physiol. 2010 Oct;299(4):H1118-23. Epub 2010 Aug 6.