

产品名称: **CX-4945 (Silmitasertib)**

产品别名: **Silmitasertib**

生物活性:

Description	Silmitasertib (CX-4945) is an orally bioavailable, highly selective and potent CK2 inhibitor, with IC ₅₀ values of 1 nM against CK2α and CK2α'.				
IC ₅₀ & Target	CK2α	CK2α'			
	1 nM (IC ₅₀)	1 nM (IC ₅₀)			
In Vitro	Silmitasertib (CX-4945) causes cell-cycle arrest and selectively induces apoptosis in cancer cells relative to normal cells, attenuates PI3K/Akt signalingand, and the antiproliferative activity of Silmitasertib (CX-4945) is correlated with expression levels of the CK2α catalytic subunit, Attenuation of PI3K/Akt signaling[1]. Silmitasertib (CX-4945) with PS-341 treatment prevents leukemic cells from engaging a functional UPR in order to buffer the PS-341-mediated proteotoxic stress in ER lumen, and decreases pro-survival ER chaperon BIP/Grp78 expression[2]. Silmitasertib (CX-4945) induces cytotoxicity and apoptosis, and exerts anti-proliferative effects in hematological tumors by downregulating CK2 expression and suppressing activation of CK2-mediated PI3K/Akt/mTOR signaling pathways[3].				
In Vivo	Silmitasertib (CX-4945) (25 or 75 mg/kg, p.o.) is well tolerated and demonstrated robust antitumor activity with concomitant reductions of the mechanism-based biomarker phospho-p21 (T145) in murine xenograft models[1].				
Solvent&Solubility	In Vitro: DMSO : ≥ 35 mg/mL (100.07 mM) 0.1 M NaOH : 33.33 mg/mL (95.29 mM); ultrasonic and adjust pH to 9 with NaOH) H ₂ O : < 0.1 mg/mL (insoluble) * "≥" means soluble, but saturation unknown.				
	Preparing Stock Solutions	<div>Solvent Concentration</div> <div>Mass</div>	1 mg	5 mg	10 mg
		1 mM	2.8590 mL	14.2951 mL	28.5902 mL
		5 mM	0.5718 mL	2.8590 mL	5.7180 mL
		10 mM	0.2859 mL	1.4295 mL	2.8590 mL
	<p>*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。</p> <p>储备液的保存方式和期限：-80℃，6 months；-20℃，1 month。 -80℃ 储存时，请在 6 个月内使用，-20℃ 储存时，请在 1 个月内使用。</p> <p>In Vivo:</p> <p>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：</p> <p>——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</p>				
	1.请依序添加每种溶剂： 10% DMSO →40% PEG300→ 5% Tween-80 → 45% saline				
	Solubility: 2.08 mg/mL (5.95 mM); Suspended solution; Need ultrasonic				
	此方案可获得 2.08 mg/mL (5.95 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。				
	以 1 mL 工作液为例，取 100 μL 20.8 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀。				

	<p>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。</p> <p>2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)</p> <p>Solubility: 2.08 mg/mL (5.95 mM); Suspended solution; Need ultrasonic</p> <p>此方案可获得 2.08 mg/mL (5.95 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。</p> <p>以 1 mL 工作液为例，取 100 μL 20.8 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。</p>
References	<p>[1]. Siddiqui-Jain A, et al. CX-4945, an orally bioavailable selective inhibitor of protein kinase CK2, inhibits prosurvival and angiogenic signaling and exhibits antitumor efficacy. <i>Cancer Res.</i> 2010 Dec 15;70(24):10288-98.</p> <p>[2]. Buontempo F, et al. Synergistic cytotoxic effects of PS-341 and CK2 inhibitor CX-4945 in acute lymphoblastic leukemia: turning off the prosurvival ER chaperone BIP/Grp78 and turning on the pro-apoptotic NF-κB. <i>Oncotarget.</i> 2016 Jan 12;7(2):1323-40.</p> <p>[3]. Chon HJ, et al. The casein kinase 2 inhibitor, CX-4945, as an anti-cancer drug in treatment of human hematological malignancies. <i>Front Pharmacol.</i> 2015 Mar 31;6:70.</p>
实验参考：	
Cell Assay	<p>Various cell lines are seeded at a density of 3,000 cells per well 24 hours prior to treatment, in appropriate media, and then treated with indicated concentrations of Silmitasertib (CX-4945). Suspensions cells are seeded and treated on the same day. Following 4 days of incubation, Alamar Blue (20 μL, 10% of volume per well) is added and the cells are further incubated at 37°C for 4-5 hours. Fluorescence with excitation wavelength at 530-560 nm and emission wavelength at 590 nm is measured. [1]</p>
Animal Administration	<p>Xenografts are initiated by subcutaneous injection of BxPC-3 cells into the right hind flank region of each mouse or BT-474 cells are injected into the mammary fat pad of mice implanted with estrogen pellets. When tumors reach a designated volume of 150-200 mm³, animals are randomized and divided into groups of 9 to 10 mice per group. Silmitasertib (CX-4945) is administered by oral gavage twice daily at 25 or 75 mg/kg for 31 and 35 consecutive days for the BT-474 and BxPC-3 models, respectively. Tumor volumes and body weights are measured twice weekly. The length and width of the tumor are measured with calipers and the volume calculated using the following formula: tumor volume=(length \times width²)/2. [1]</p>
References	<p>[1]. Siddiqui-Jain A, et al. CX-4945, an orally bioavailable selective inhibitor of protein kinase CK2, inhibits prosurvival and angiogenic signaling and exhibits antitumor efficacy. <i>Cancer Res.</i> 2010 Dec 15;70(24):10288-98.</p> <p>[2]. Buontempo F, et al. Synergistic cytotoxic effects of PS-341 and CK2 inhibitor CX-4945 in acute lymphoblastic leukemia: turning off the prosurvival ER chaperone BIP/Grp78 and turning on the pro-apoptotic NF-κB. <i>Oncotarget.</i> 2016 Jan 12;7(2):1323-40.</p> <p>[3]. Chon HJ, et al. The casein kinase 2 inhibitor, CX-4945, as an anti-cancer drug in treatment of human hematological malignancies. <i>Front Pharmacol.</i> 2015 Mar 31;6:70.</p>