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产品名称：CX-4945 (sodium salt)
产品别名：Silmitasertib sodium salt

生物活性：

Description	Silmitasertib sodium salt 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:

H_2O : 16.67 mg/mL (44.84 mM; Need ultrasonic)

DMSO : 6.67 mg/mL (17.94 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.6900 mL	13.4499 mL	26.8998 mL
5 mM	0.5380 mL	2.6900 mL	5.3800 mL
10 mM	0.2690 mL	1.3450 mL	2.6900 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:

1.CX-4945 sodium salt is dissolved in 25 mM sodium phosphate buffer (pH=4.3) [4].

References

[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. Cancer Res. 2010 Dec 15;70(24):10288-98.

[2]. Kendall JJ, et al. CK2 blockade causes MPNST cell apoptosis and promotes degradation of β-catenin. Oncotarget. 2016 Aug 16;7(33):53191-53203.

[3]. 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. Oncotarget. 2016 Jan 12;7(2):1323-40.

	[4]. Chon HJ, et al. The casein kinase 2 inhibitor, CX-4945, as an anti-cancer drug in treatment of human hematological malignancies. Front Pharmacol. 2015 Mar 31;6:70.

实验参考：

Cell Assay	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].
Animal Administration	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 mm^3, 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 × $width^2$)/2. [1]
References	[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. Cancer Res. 2010 Dec 15;70(24):10288-98. [2]. Kendall JJ, et al. CK2 blockade causes MPNST cell apoptosis and promotes degradation of β-catenin. Oncotarget. 2016 Aug 16;7(33):53191-53203. [3]. 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. Oncotarget. 2016 Jan 12;7(2):1323-40. [4]. Chon HJ, et al. The casein kinase 2 inhibitor, CX-4945, as an anti-cancer drug in treatment of human hematological malignancies. Front Pharmacol. 2015 Mar 31;6:70.