产品名称：CEP-18770 (Delanzomib)
产品别名：Delanzomib

生物活性：

Description

Delanzomib(CEP-18770) is a novel orally-active inhibitor of the chymotrypsin-like activity of the proteasome that down-modulates the nuclear factor-kappaB (NF-kappaB) activity. IC50 Value: 3.8 nM [1] Target: proteasome in vitro: CEP-18770 and bortezomib showed comparable potency against chymotrypsin-like proteasome activity, cellular inhibitory activity (IC50) values of 3.8 (± 1.0) nM and 3.8 (± 0.4) nM, respectively, CEP-18770 had a 2- to 11-fold lower cytotoxic potency compared with bortezomib against solid tumor cell lines, comparable potency against 2 hematologic tumor cell lines, and a similar spectrum of antiproliferative activity with IC50 values for both compounds of less than 35 nM [1]. in vivo: in MM xenograft models, the addition of CEP-18770 IV to melphalan completely prevented the growth of both melphalan-sensitive and melphalan-resistant tumours. The combination of CEP-18770 IV and bortezomib induced complete regression of bortezomib-sensitive tumours and markedly delayed progression of bortezomib-resistant tumours compared to treatment with either agent alone [2]. Age matched MRL/lpr or NZBWF1 mice with established SLE or LN, respectively, were treated with delanzomib either 3 mg/kg once or twice weekly intravenously or orally at 10 mg/kg [3]. Toxicity: CEP-18770 showed a favourable safety profile with lack of neurotoxicity and linear plasma PK. The definition of the optimal biological dose and schedule of treatment is actively pursued because of the high incidence of skin toxicity of the twice a week schedule [4]. Clinical trial: CEP-18770 in Combination With Lenalidomide and Dexamethasone in Relapsed or Refractory Multiple Myeloma. Phase1/2

Solvent&Solubility

In Vitro:

DMSO : 130 mg/mL (314.56 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4197 mL	12.0983 mL	24.1967 mL
	5 mM	0.4839 mL	2.4197 mL	4.8393 mL
	10 mM	0.2420 mL	1.2098 mL	2.4197 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: ≥ 2.17 mg/mL (5.25 mM); Clear solution

此方案可获得 ≥ 2.17 mg/mL (5.25 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 21.7 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: 2.17 mg/mL (5.25 mM); Suspended solution; Need ultrasonic 此方案可获得 2.17 mg/mL (5.25 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 21.7 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: ≥ 2.17 mg/mL (5.25 mM); Clear solution 此方案可获得 ≥ 2.17 mg/mL (5.25 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 21.7 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Piva R, et al. CEP-18770: A novel, orally active proteasome inhibitor with a tumor-selective pharmacologic profile competitive with bortezomib. Blood. 2008 Mar 1;111(5):2765-75. [2]. Sanchez E, et al. The proteasome inhibitor CEP-18770 enhances the anti-myeloma activity of bortezomib and melphalan. Br J Haematol. 2010 Feb;148(4):569-81. [3]. Seavey MM, et al. Novel, orally active, proteasome inhibitor, delanzomib (CEP-18770), ameliorates disease symptoms and glomerulonephritis in two preclinical mouse models of SLE. Int Immunopharmacol. 2012 Jan;12(1):257-70. [4]. Gallerani E, et al. A first in human phase I study of the proteasome inhibitor CEP-18770 in patients with advanced solid tumours and multiple myeloma. Eur J Cancer. 2013 Jan;49(2):290-6.