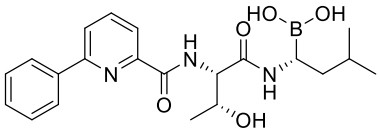
Product data sheet

MedKoo Cat#: 200713 Name: Delanzomib (CEP-18770) CAS#: 847499-27-8 Chemical Formula: $C_{21}H_{28}BN_3O_5$ Exact Mass: 413.2122 Molecular Weight: 413.27	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

Delanzomib, also known as CEP-18770, is An orally bioavailable synthetic P2 threonine boronic acid inhibitor of the chymotrypsin-like activity of the proteasome, with potential antineoplastic activity. Proteasome inhibitor CEP 18770 represses the proteasomal degradation of a variety of proteins, including inhibitory kappaBalpha (IkappaBalpha), resulting in the cytoplasmic sequestration of the transcription factor NF-kappaB; inhibition of NF-kappaB nuclear translocation and transcriptional up-regulation of a variety of cell growth-promoting factors; and apoptotic cell death in susceptible tumor cell populations.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	71.0	171.80
DMF	30.0	72.59
Ethanol	56.5	136.71

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.42 mL	12.10 mL	24.20 mL
5 mM	0.48 mL	2.42 mL	4.84 mL
10 mM	0.24 mL	1.21 mL	2.42 mL
50 mM	0.05 mL	0.24 mL	0.48 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Eleftheriadis T, Pissas G, Antoniadi G, Liakopoulos V, Stefanidis I. Proteasome or immunoproteasome inhibitors cause apoptosis in human renal tubular epithelial cells under normoxic and hypoxic conditions. Int Urol Nephrol. 2016 Jun;48(6):907-15. doi: 10.1007/s11255-016-1247-6. Epub 2016 Feb 26. PMID: 26920131.
2. Li J, Zhuo JY, Zhou W, Hong JW, Chen RG, Xie HY, Zhou L, Zheng SS, Jiang DH. Endoplasmic reticulum stress triggers delanzomib-induced apoptosis in HCC cells through the PERK/eIF2α/ATF4/CHOP pathway. Am J Transl Res. 2020 Jun 15;12(6):2875-2889. PMID: 32655816; PMCID: PMC7344101.

In vivo study

1. Seavey MM, Lu LD, Stump KL, Wallace NH, Ruggeri BA. 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. doi: 10.1016/j.intimp.2011.11.019. Epub 2011 Dec 13. PMID: 22178195.

2. Li J, Zhuo JY, Zhou W, Hong JW, Chen RG, Xie HY, Zhou L, Zheng SS, Jiang DH. Endoplasmic reticulum stress triggers delanzomib-induced apoptosis in HCC cells through the PERK/eIF2α/ATF4/CHOP pathway. Am J Transl Res. 2020 Jun 15;12(6):2875-2889. PMID: 32655816; PMCID: PMC7344101.

7. Bioactivity

Biological target:

Delanzomib (CEP-18770) is a chymotrypsin-like activity of the proteasome inhibitor with an IC50 of 3.8 nM.

In vitro activity

As shown in Figure 4C, delanzomib could up-regulate ERS-associated proteins in a concentration-dependent manner in both sorafenib sensitive and resistant HCC cells. After treatment with delanzomib on SK-hep-1 and SK-sora-5 cells for 48 h, the protein levels of p-PERK and p-eIF2α were significantly increased, whereas total PERK and eIF2α remained unchanged. Moreover, the protein levels of ATF4 and CHOP were also increased (The Original image of WB scan is shown in the Supplementary Figure 5). To further verify the role of ERS in delanzomib-induced apoptosis, salubrinal as a selective inhibitor of eIF2α dephosphorylation, was adopted to co-treated HCC cells with delanzomib. Interestingly, salubrinal significantly reduced delanzomib-induced apoptosis in both HCC cells (Figure 4D). The ratio of apoptotic cells decreased from 25.7% to 12.3% for SK-hep-1 ($P<0.01$) and from 22.8% to 11.5% for SK-sora-5 ($P<0.01$), respectively. All these data demonstrated that delanzomib could induce the activation of ERS, and ERS could trigger delanzomib-induced apoptosis through the PERK/eIF2α/ATF4/CHOP pathway in HCC cells despite they were sensitive or resistant to sorafenib.

Reference: Am J Transl Res. 2020; 12(6): 2875–2889. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7344101/

In vivo activity

Treatment of SLE-prone, proteinuria-positive NZM mice with delanzomib extended survival significantly over vehicle (55% and 46% respectively; $p < 0.001$) and significantly extended survival over that of both CTX and both bortezomib treatment groups ($p < 0.01$) (Fig. S3D) ($p < 0.001$). Both 20S proteasome activity and IκBα accumulation were used as pharmacodynamic indicators of delanzomib-mediated proteasome inhibition in the spleen and kidneys of treated NZM mice. Once and twice weekly administration of delanzomib inhibited spleen 20S proteasome activity as compared to vehicle treatment ($p < 0.05$) (40% inhibition relative to vehicle) (Fig. S4A). Twice, but not once, weekly administration of delanzomib increased the accumulation of kidney IκBα levels above that of the vehicle-treatment (40% increase, $p < 0.05$) (Fig. S4B).

Reference: Int Immunopharmacol. 2012 Jan;12(1):257-70. https://pubmed.ncbi.nlm.nih.gov/22178195/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.