Product data sheet



MedKoo Cat#: 206846				
Name: Ciforadenant				
CAS#: 1202402-40-1				
Chemical Formula: $C_{20}H_{21}N_7O_3$				
Exact Mass: 407.1706				
Molecular Weight: 407.43				
Product supplied as:	Powder			
Purity (by HPLC):	$\geq 98\%$			
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:

Ciforadenant, also known as CPI-444 and V81444, is an orally administered antagonist of the adenosine A2A receptor. Upon oral administration, CPI-444 binds to adenosine A2A receptors expressed on the surface of immune cells, including T-lymphocytes, natural killer (NK) cells, macrophages and dendritic cells (DCs). This prevents tumor-released adenosine from interacting with the A2A receptors on these key immune surveillance cells, thereby abrogating adenosine-induced immunosuppression in the tumor microenvironment.

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	74.25	182.24

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.45 mL	12.27 mL	24.54 mL
5 mM	0.49 mL	2.45 mL	4.91 mL
10 mM	0.25 mL	1.23 mL	2.45 mL
50 mM	0.05 mL	0.25 mL	0.49 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. Willingham SB, Ho PY, Hotson A, Hill C, Piccione EC, Hsieh J, Liu L, Buggy JJ, McCaffery I, Miller RA. A2AR Antagonism with CPI-444 Induces Antitumor Responses and Augments Efficacy to Anti-PD-(L)1 and Anti-CTLA-4 in Preclinical Models. Cancer Immunol Res. 2018 Oct;6(10):1136-1149. doi: 10.1158/2326-6066.CIR-18-0056. Epub 2018 Aug 21. PMID: 30131376.

In vivo study

1. Willingham SB, Ho PY, Hotson A, Hill C, Piccione EC, Hsieh J, Liu L, Buggy JJ, McCaffery I, Miller RA. A2AR Antagonism with CPI-444 Induces Antitumor Responses and Augments Efficacy to Anti-PD-(L)1 and Anti-CTLA-4 in Preclinical Models. Cancer Immunol Res. 2018 Oct;6(10):1136-1149. doi: 10.1158/2326-6066.CIR-18-0056. Epub 2018 Aug 21. PMID: 30131376.

7. Bioactivity

Biological target: CPI-444 (V81444) is an adenosine A2A receptor (A2AR) antagonist.

In vitro activity

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Activated T cells have high expression of A2AR, and NECA-mediated activation of A2AR increased cAMP in human T cells (Fig. 2A), consistent with previous reports (13, 36–38). Inclusion of CPI-444 led to a dose-dependent inhibition of the production of intracellular cAMP following stimulation of activated primary human T cells with NECA (IC50 = 70 nmol/L; Fig. 2A). CPI-444 completely inhibited NECA-mediated elevation of cAMP in these human PBMC cultures, suggesting that A2AR is the dominant adenosine receptor that mediates immune suppression in this system. Elevated intracellular cAMP following A2AR activation results in the phosphorylation of CREB (cAMP response element-binding protein; ref. 39). CPI-444 treatment inhibited phosphorylation of CREB (pCREB; Supplementary Fig. S1A) in NECA-stimulated cells. These results demonstrate that CPI-444 restores T-cell signaling in the presence of adenosine analogues.

Reference: Cancer Immunol Res. 2018 Oct;6(10):1136-1149. https://cancerimmunolres.aacrjournals.org/content/6/10/1136.long

In vivo activity

MC38 is a mouse colon carcinoma cell line that is responsive to immune checkpoint blockade, including anti–PD-1 antibodies (28, 29). To evaluate the antitumor efficacy of CPI-444 in vivo, MC38 cells were engrafted onto the backs of syngeneic C57BL/6 mice. One day after tumor cell engraftment, vehicle control solution or CPI-444 (1, 10, or 100 mg/kg) was administered daily via oral gavage for 28 days (see Supplementary Table S2 for details of all animal experiments). Administration of CPI-444 at 10 mg/kg and 100 mg/kg resulted in a significant inhibition of tumor growth, whereas 1 mg/kg had no discernable effect compared with vehicle-treated animals (Fig. 3A and Supplementary Fig. S2A–S2C for spider plots of individual mice). Complete tumor regression was observed in 9 of 29 mice treated with CPI-444 (Supplementary Fig. S2D). Tumor growth was fully inhibited when mice with cleared tumors were later rechallenged, indicating that CPI-444 induced systemic antitumor immune memory.

Reference: Cancer Immunol Res. 2018 Oct;6(10):1136-1149. https://cancerimmunolres.aacrjournals.org/content/6/10/1136.long

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.