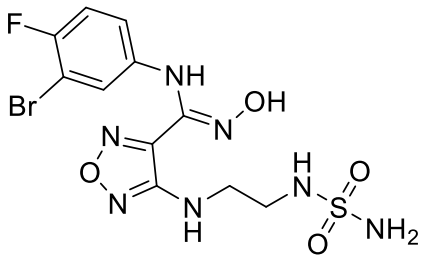
Product data sheet

MedKoo Cat#: 206461 Name: Epacadostat (INCB024360) CAS#: 1204669-58-8 (INCB024360) Chemical Formula: $C_{11}H_{13}BrFN_7O_4S$ Exact Mass: 436.99171 Molecular Weight: 438.23	
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:
Epacadostat, also known as INCB024360, is an orally available hydroxyamidine and inhibitor of indoleamine 2,3-dioxygenase (IDO1), with potential immunomodulating and antineoplastic activities. INCB024360 targets and binds to IDO1, an enzyme responsible for the oxidation of tryptophan into kynurenine. By inhibiting IDO1 and decreasing kynurenine in tumor cells, INCB024360 increases and restores the proliferation and activation of various immune cells, including dendritic cells (DCs), NK cells, and T-lymphocytes, as well as interferon (IFN) production, and a reduction in tumor-associated regulatory T cells (Tregs).

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	87	198.53
Ethanol	87	198.53

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.28 mL	11.41 mL	22.82 mL
5 mM	0.46 mL	2.28 mL	4.56 mL
10 mM	0.23 mL	1.14 mL	2.28 mL
50 mM	0.05 mL	0.23 mL	0.46 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. Liu X, Shin N, Koblish HK, Yang G, Wang Q, Wang K, Leffet L, Hansbury MJ, Thomas B, Rupar M, Waeltz P, Bowman KJ, Polam P, Sparks RB, Yue EW, Li Y, Wynn R, Fridman JS, Burn TC, Combs AP, Newton RC, Scherle PA. Selective inhibition of IDO1 effectively regulates mediators of antitumor immunity. Blood. 2010 Apr 29;115(17):3520-30. doi: 10.1182/blood-2009-09-246124. Epub 2010 Mar 2. PMID: 20197554.

In vivo study

1. Liu X, Shin N, Koblish HK, Yang G, Wang Q, Wang K, Leffet L, Hansbury MJ, Thomas B, Rupar M, Waeltz P, Bowman KJ, Polam P, Sparks RB, Yue EW, Li Y, Wynn R, Fridman JS, Burn TC, Combs AP, Newton RC, Scherle PA. Selective inhibition of IDO1 effectively regulates mediators of antitumor immunity. Blood. 2010 Apr 29;115(17):3520-30. doi: 10.1182/blood-2009-09-246124. Epub 2010 Mar 2. PMID: 20197554.

2. Koblish HK, Hansbury MJ, Bowman KJ, Yang G, Neilan CL, Haley PJ, Burn TC, Waeltz P, Sparks RB, Yue EW, Combs AP, Scherle PA, Vaddi K, Fridman JS. Hydroxyamidine inhibitors of indoleamine-2,3-dioxygenase potently suppress systemic tryptophan

catabolism and the growth of IDO-expressing tumors. Mol Cancer Ther. 2010 Feb;9(2):489-98. doi: 10.1158/1535-7163.MCT-09-0628. Epub 2010 Feb 2. PMID: 20124451.

7. Bioactivity

Biological target:

Epacadostat (INCB024360) is a potent and selective indoleamine 2,3-dioxygenase (IDO1) inhibitor with IC50 of 10 nM and displays high selectivity over other related enzymes such as IDO2 or tryptophan 2,3-dioxygenase (TDO).

In vitro activity

In cellular assays, INCB024360 selectively inhibits human IDO1 with IC(50) values of approximately 10nM, demonstrating little activity against other related enzymes such as IDO2 or tryptophan 2,3-dioxygenase (TDO). In coculture systems of human allogeneic lymphocytes with dendritic cells (DCs) or tumor cells, INCB024360 inhibition of IDO1 promotes T and natural killer (NK)-cell growth, increases IFN-gamma production, and reduces conversion to regulatory T (T(reg))-like cells. IDO1 induction triggers DC apoptosis, whereas INCB024360 reverses this and increases the number of CD86(high) DCs, potentially representing a novel mechanism by which IDO1 inhibition activates T cells. Furthermore, IDO1 regulation differs in DCs versus tumor cells.

Reference: Blood. 2010 Apr 29;115(17):3520-30. https://linkinghub.elsevier.com/retrieve/pii/S0006-4971(20)35093-X

In vivo activity

To investigate whether IDO1 inhibition would similarly reverse immune escape in vivo, bearing IDO1-expressing PAN02 pancreatic carcinomas were treated orally with INCB024360. The growth of tumors in syngeneic immunocompetent C57BL/6 mice was inhibited in a dose-dependent fashion, with 37% and 57% TGC, respectively, for 25 and 100 mg/kg INCB024360 (Figure 5A; P < .01). However, tumors growing in immunodeficient Balb/c nu/nu mice were not affected by similar doses of INCB024360 (Figure 5B). The inability of INCB024360 to elicit an antitumor response in the immunodeficient mice was not due to lesser impact on kyn generation, as the compound levels were similar between the 2 strains and kyn-to-trp ratios were, in fact, more affected in the immunodeficient mice (Figure 5C). Therefore, consistent with the proposed mechanism of action, INCB024360 suppresses kyn generation in vivo, and its antitumor activity is mediated by lymphocytes.

Reference: Blood. 2010 Apr 29;115(17):3520-30. https://linkinghub.elsevier.com/retrieve/pii/S0006-4971(20)35093-X