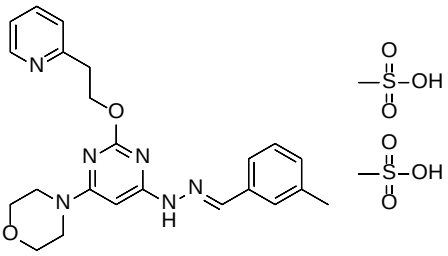
Product data sheet

MedKoo Cat#: 407105 Name: Apilimod mesylate CAS#: 870087-36-8 (mesylate) Chemical Formula: $C_{25}H_{34}N_6O_8S_2$ Molecular Weight: 610.70	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

Apilimod, also known as STA-5326, is a IL-12/IL-23 inhibitor. Apilimod inhibits IL-12 and IL-23 production - cytokines that are involved in autoimmune diseases - through the prevention of nuclear translocation of c-Rel. Synta Pharmaceuticals Corp is developing apilimod for the potential treatment of Crohn's disease (CD) and other autoimmune diseases. Preclinical studies demonstrated the successful inhibition of IL-12 and IL-23 production by the drug.

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
Water	87.02	142.49
DMSO	31.01	50.78
Ethanol	2.50	4.09

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.64 mL	8.19 mL	16.37 mL
5 mM	0.33 mL	1.64 mL	3.27 mL
10 mM	0.16 mL	0.82 mL	1.64 mL
50 mM	0.03 mL	0.16 mL	0.33 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. Gayle S, Landrette S, Beeharry N, Conrad C, Hernandez M, Beckett P, Ferguson SM, Mandelkern T, Zheng M, Xu T, Rothberg J, Lichenstein H. Identification of apilimod as a first-in-class PIKfyve kinase inhibitor for treatment of B-cell non-Hodgkin lymphoma. Blood. 2017 Mar 30;129(13):1768-1778. doi: 10.1182/blood-2016-09-736892. Epub 2017 Jan 19. PMID: 28104689; PMCID: PMC5766845.

2. Sbrissa D, Naisan G, Ikonomov OC, Shisheva A. Apilimod, a candidate anticancer therapeutic, arrests not only PtdIns(3,5)P2 but also PtdIns5P synthesis by PIKfyve and induces bafilomycin A1-reversible aberrant endomembrane dilation. PLoS One. 2018 Sep 21;13(9):e0204532. doi: 10.1371/journal.pone.0204532. PMID: 30240452; PMCID: PMC6150535.

In vivo study

1. Gayle S, Landrette S, Beeharry N, Conrad C, Hernandez M, Beckett P, Ferguson SM, Mandelkern T, Zheng M, Xu T, Rothberg J, Lichenstein H. Identification of apilimod as a first-in-class PIKfyve kinase inhibitor for treatment of B-cell non-Hodgkin lymphoma. Blood. 2017 Mar 30;129(13):1768-1778. doi: 10.1182/blood-2016-09-736892. Epub 2017 Jan 19. PMID: 28104689; PMCID: PMC5766845.

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7. Bioactivity

Biological target: Apilimod mesylate is an IL-12/IL-23 inhibitor which inhibits IL-12 with IC50s of 1 nM and 2 nM, in IFN-γ/SAC-stimulated human PBMCs and SAC-treated monkey PBMCs, respectively.

In vitro activity

To determine whether apilimod induced cytotoxicity in cancer cells, B-NHL was costained with Annexin V, a marker for early apoptosis, and 7-AAD, a membrane-impermeant marker of nonviable cells. A marked loss of membrane integrity and increased Annexin V staining was observed in apilimod-treated B-NHL, confirming induction of cell death (Figure 3A; supplemental Figure 6A). No marked increases in DEVD-UltraGlo Luciferase cleavage (surrogate for caspase 3/7 activity) were observed in apilimod-treated B-NHL cells at physiologically relevant concentrations (Figure 3B; supplemental Figure 6B), nor were a significant rescue of cell viability with caspase, cathepsin, or necroptosis inhibitors observed across the cell lines tested (Figures 3C-3E; supplemental Figure 6C-E). Interestingly, apilimod appears to disrupt the completion of autophagy as indicated by an increase in the levels of p62 and LC3-II (Figure 3F; supplemental Figure 6F). These data suggest that apilimod blocks autophagy and its effects are distinct from apoptosis, lysosomal membrane permeabilization, and necroptosis.

Reference: Blood. 2017 Mar 30;129(13):1768-1778. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5766845/

In vivo activity

The effects of apilimod were tested in in vivo models of lymphoma. With oral dosing of 60 mg/kg apilimod dimesylate (~41 mg/kg apilimod free base; twice a day), 48% tumor growth inhibition was observed in the SU-DHL-6 model. Further evaluation of apilimod in an immunocompetent A20 syngeneic lymphoma model provided the opportunity to investigate apilimod in combination with the immuno-oncology therapeutic, anti-programmed death ligand 1 (PD-L1). Apilimod showed significant synergism in the A20 model, manifesting as 86% tumor growth inhibition for the combination with anti-PD-L1, compared with 51% and 53% in the apilimod and anti-PD-L1 single arms, respectively (Figure 2C).

Reference: Blood. 2017 Mar 30;129(13):1768-1778. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5766845/