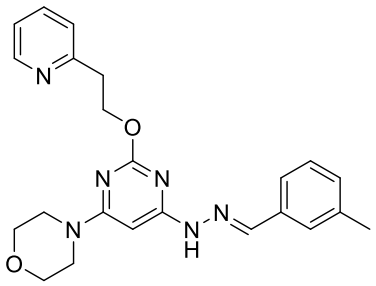
Product data sheet

MedKoo Cat#: 326647 Name: Apilimod free base CAS#: 541550-19-0 (free base) Chemical Formula: $C_{23}H_{26}N_6O_2$ Exact Mass: 418.2117 Molecular Weight: 418.501	
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:

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
DMSO	46	109.92

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.39 mL	11.95 mL	23.89 mL
5 mM	0.48 mL	2.39 mL	4.78 mL
10 mM	0.24 mL	1.19 mL	2.39 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. 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.

In vivo study

1. Wada Y, Lu R, Zhou D, Chu J, Przewloka T, Zhang S, Li L, Wu Y, Qin J, Balasubramanyam V, Barsoum J, Ono M. Selective abrogation of Th1 response by STA-5326, a potent IL-12/IL-23 inhibitor. Blood. 2007 Feb 1;109(3):1156-64. doi: 10.1182/blood-2006-04-019398. Epub 2006 Oct 19. PMID: 17053051.

2. Cinato M, Guitou L, Saidi A, Timotin A, Sperazza E, Duparc T, Zolov SN, Giridharan SSP, Weisman LS, Martinez LO, Roncalli J, Kunduzova O, Tronchere H, Boal F. Apilimod alters TGFβ signaling pathway and prevents cardiac fibrotic remodeling. Theranostics. 2021 Apr 19;11(13):6491-6506. doi: 10.7150/thno.55821. PMID: 33995670; PMCID: PMC8120213.

7. Bioactivity

Product data sheet

Biological target:

Apilimod (STA 5326) is a potent IL-12/IL-23 inhibitor, and strongly 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

Apilimod was profiled for its antiproliferative activity against 146 cell lines representing 11 tumor types. Although cells from many cancer lineages responded to apilimod, it was observed that B-NHL lines were the most broadly sensitive (supplemental Figure 2). We noted antiproliferative activity in all B-NHL subtypes with ~73% of lines having an IC50 < 200 nM (Figure 1A) and defined these as sensitive. Notably, significant antiproliferative activity was observed on cell lines derived from difficult to treat double- and triple-hit B-NHL. Although apilimod was initially identified through screening of an mTORC1-hyperactivated cell line, potent antiproliferative activity in B-NHL lines irrespective of mTORC1 activation were observed (supplemental Table 1; supplemental Figure 3). Furthermore, apilimod did not affect mTORC1 signaling (supplemental Figure 3B). Overall, apilimod had selective antiproliferative activity for B-NHL compared with normal cells with IC50 of 142 nM and 12 782 nM, respectively (Figure 1B-C; see supplemental Tables 1 and 2 for cell line–specific data in lymphoma and normal cells).

Reference: Blood. 2017 Mar 30;129(13):1768-1778. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/28104689/

In vivo activity

To address the effects of Apilimod in cardiac fibrotic remodeling, a mouse model of transverse aortic constriction (TAC) was used. Cardiac pressure overload induced by four weeks TAC triggered a massive myocardial deposition of ECM proteins as shown by Sirius red staining, typical for end-stage fibrotic tissue remodeling (Figure 1A-B). Strikingly, Apilimod abrogated myocardial collagen fibre accumulation in TAC-mice (Figure 1A-B). Consistently, daily Apilimod treatment attenuated TAC-induced overexpression of cardiac pro-fibrotic genes including collagen 1 (Col1, Figure 1C), collagen 3 (Col3, Figure 1D), fibronectin 1 (Figure 1E) and connective tissue growth factor (Ctgf, Figure 1F). Moreover, upon Apilimod treatment, TAC-induced expression of periostin, a well-known marker of activated cardiac fibroblasts 29, was strongly inhibited (Figure 1G), suggesting that Apilimod prevents fibroblast activation in vivo. Consistently, TAC-stressed mice treated with Apilimod showed reduced level of α-SMA as demonstrated by immunofluorescent staining (Figure S1A). Moreover, we found that Apilimod decreased the recruitment of CD-68-positive macrophages (Figure S1B) and the production of the myocardial pro-inflammatory cytokines Il-6 (Figure S1C), Tnf-α (Figure S1D) and Ccl2 (Figure S1E). In addition, we found that Apilimod reduced cardiac hypertrophy induced by TAC, as shown morphologically (Figure 2A-B) and by the expression of the hypertrophic markers Anp (Figure 2C), Bnp (Figure 2D), α-skeletal actin (Figure 2E) and β-Mhc (Figure 2F). Consistently, echocardiography analysis showed that Apilimod reduced end-diastolic ventricular wall thickness, intraventricular septum thickness and left ventricular mass (Table 1) in TAC-stressed mice hearts. It has to be noted that Apilimod-treatment does not completely abrogate the hypertrophic response following TAC. Importantly, the myocardial anti-fibrotic effect of Apilimod culminated in the preservation of cardiac function in TAC-mice, as shown by improved EF and shortening fraction (Table 1 and Figure S1F, EF and SF respectively). These results suggest that Apilimod is a potent inhibitor of fibroblast activation and myocardial fibrosis development in vivo, leading to preserved cardiac performance following TAC surgery.

Reference: Theranostics. 2021 Apr 19;11(13):6491-6506. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/33995670/