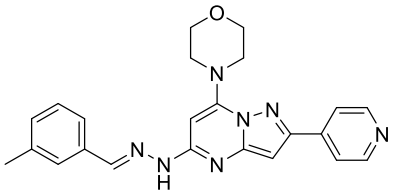
Product data sheet

MedKoo Cat#: 522383 Name: APY0201 CAS#: 1232221-74-7 Chemical Formula: $C_{23}H_{23}N_7O$ Exact Mass: 413.19641 Molecular Weight: 413.48	
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:
APY0201 is a potent and selective IL-12/23 inhibitor. APY0201 demonstrates ameliorated inflammation in an experimental model of colitis. Interleukin-12 (IL-12) and IL-23 are proinflammatory cytokines and therapeutic targets for inflammatory and autoimmune diseases, including inflammatory bowel diseases, psoriasis, rheumatoid arthritis, and multiple sclerosis.

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	20.0	48.37
DMSO:PBS (pH 7.2) (1:2)	0.33	0.80
DMF	3.0	7.26

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.42 mL	12.09 mL	24.18 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. de Campos CB, Zhu YX, Sepetov N, Romanov S, Bruins LA, Shi CX, Stein CK, Petit JL, Polito AN, Sharik ME, Meermeier EW, Ahmann GJ, Armenta IDL, Kruse J, Bergsagel PL, Chesi M, Meurice N, Braggio E, Stewart AK. Identification of PIKfyve kinase as a target in multiple myeloma. Haematologica. 2020 Jun;105(6):1641-1649. doi: 10.3324/haematol.2019.222729. Epub 2019 Oct 3. PMID: 31582538; PMCID: PMC7271606.
2. Hayakawa N, Noguchi M, Takeshita S, Eviryanti A, Seki Y, Nishio H, Yokoyama R, Noguchi M, Shuto M, Shima Y, Kuribayashi K, Kageyama S, Eda H, Suzuki M, Hatta T, Iemura S, Natsume T, Tanabe I, Nakagawa R, Shiozaki M, Sakurai K, Shoji M, Andou A, Yamamoto T. Structure-activity relationship study, target identification, and pharmacological characterization of a small molecular IL-12/23 inhibitor, APY0201. Bioorg Med Chem. 2014 Jun 1;22(11):3021-9. doi: 10.1016/j.bmc.2014.03.036. Epub 2014 Apr 13. PMID: 24767819.

In vivo study

1. Hayakawa N, Noguchi M, Takeshita S, Eviryanti A, Seki Y, Nishio H, Yokoyama R, Noguchi M, Shuto M, Shima Y, Kuribayashi K, Kageyama S, Eda H, Suzuki M, Hatta T, Iemura S, Natsume T, Tanabe I, Nakagawa R, Shiozaki M, Sakurai K, Shoji M, Andou A,

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Yamamoto T. Structure-activity relationship study, target identification, and pharmacological characterization of a small molecular IL-12/23 inhibitor, APY0201. Bioorg Med Chem. 2014 Jun 1;22(11):3021-9. doi: 10.1016/j.bmc.2014.03.036. Epub 2014 Apr 13. PMID: 24767819.

7. Bioactivity

Biological target:

APY0201 is a PIKfyve inhibitor, which inhibits the conversion of PtdIns3P to PtdIns(3,5)P2 in the presence of [^{33}P]ATP with an IC50 of 5.2 nM. APY0201 also inhibits IL-12/IL-23 production.

In vitro activity

Following treatment with APY0201 for 6 h, activation of TFEB, found in its dephosphorylated state, was observed independently of the HMCL sensitivity profile to the compound. Nuclear translocation of TFEB following PIKfyve exposure was subsequently confirmed in a subcellular localization immunoblotting assay (Figure 2C, D). Dephosphorylated TFEB translocates from the cytoplasm to the nucleus to regulate the expression of target genes associated with autophagy. Therefore, these findings further supported an APY0201-induced autophagy disturbance through PIKfyve inhibition in MM.

Reference: Haematologica. 2020 Jun; 105(6): 1641–1649. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7271606/

In vivo activity

To determine the impact of PIFKfyve inhibition on inflammatory responses in vivo, this study evaluated APY0201 in a mouse model of inflammatory bowel disease (IBD) induced by the adoptive transfer of IL-10 knockout (KO) CD4+ T cells. An increase in the colon weight ratio was observed in the vehicle control group for colitis compared with that in the normal control group. Daily administration of APY0201 significantly reduced increases in colon weight in a dose-dependent manner (Fig. 7a; 19.7%, 25.4%, and 73.3% reduction at 3, 10, and 30 mg/kg, respectively), and the effect of APY0201 at 30 mg/kg was equivalent to that of prednisolone (PSL) at 15 mg/kg B.I.D. (81.0% reduction, Fig. 7b). Examination of the stool consistency showed that the vehicle control group exhibited severe diarrhea on the day of the sacrifice, while APY0201 significantly prevented development of diarrhea in a dose-dependent manner (Fig. 7c and d). Twice a day administration of PSL ameliorated inflammation in this mouse model of colitis. However, treatment with PSL led to a significant decrease in body weight after chronic administration relative to that of the vehicle or normal control groups, although the drug relieved diarrhea and reduced colon weight (please see the Supplementary information). Conversely, administration of APY0201 caused no difference in body weight relative to that of the normal control group. These results clearly demonstrated that APY0201 was orally available and significantly efficacious in a mouse model of colitis induced by adoptive transfer of IL-10 KO CD4+ T cells without showing any sign of adverse effects.

Reference: Bioorg Med Chem. 2014 Jun 1;22(11):3021-9. https://pubmed.ncbi.nlm.nih.gov/24767819/