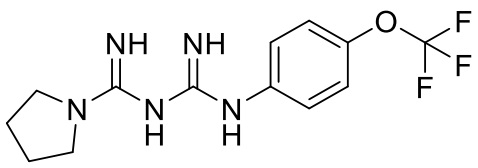
Product data sheet

MedKoo Cat#: 207129 Name: IM156 CAS#: 1422365-93-2 (free base) Chemical Formula: $C_{13}H_{16}F_3N_5O$ Exact Mass: 315.1307 Molecular Weight: 315.3002	
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:
IM156 is an oxidative phosphorylation inhibitor. IM156 is an orally bioavailable biguanide compound and mitochondrial oxidative phosphorylation (OxPhos) inhibitor, with potential antineoplastic activity. Upon administration, IM156 inhibits oxidative phosphorylation, decreases mitochondrial function, prevents tumor cell metabolism and deprives tumor cells of energy, thereby preventing tumor cell proliferation.

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	30.0	95.15
Ethanol	20.0	63.43

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.17 mL	15.86 mL	31.72 mL
5 mM	0.63 mL	3.17 mL	6.34 mL
10 mM	0.32 mL	1.59 mL	3.17 mL
50 mM	0.06 mL	0.32 mL	0.63 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. Izreig S, Gariepy A, Kaymak I, Bridges HR, Donayo AO, Bridon G, DeCamp LM, Kitchen-Goosen SM, Avizonis D, Sheldon RD, Laister RC, Minden MD, Johnson NA, Duchaine TF, Rudoltz MS, Yoo S, Pollak MN, Williams KS, Jones RG. Repression of LKB1 by miR-17~92 Sensitizes MYC-Dependent Lymphoma to Biguanide Treatment. Cell Rep Med. 2020 May 19;1(2):100014. doi: 10.1016/j.xcrm.2020.100014. PMID: 32478334; PMCID: PMC7249503.
2. Son J, Cho YW, Woo YJ, Baek YA, Kim EJ, Cho Y, Kim JY, Kim BS, Song JJ, Ha SJ. Metabolic Reprogramming by the Excessive AMPK Activation Exacerbates Antigen-Specific Memory CD8+ T Cell Differentiation after Acute Lymphocytic Choriomeningitis Virus Infection. Immune Netw. 2019 Mar 5;19(2):e11. doi: 10.4110/in.2019.19.e11. PMID: 31089438; PMCID: PMC6494768.

In vivo study

1. Son J, Cho YW, Woo YJ, Baek YA, Kim EJ, Cho Y, Kim JY, Kim BS, Song JJ, Ha SJ. Metabolic Reprogramming by the Excessive AMPK Activation Exacerbates Antigen-Specific Memory CD8+ T Cell Differentiation after Acute Lymphocytic Choriomeningitis Virus Infection. Immune Netw. 2019 Mar 5;19(2):e11. doi: 10.4110/in.2019.19.e11. PMID: 31089438; PMCID: PMC6494768.

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2. Izreig S, Gariepy A, Kaymak I, Bridges HR, Donayo AO, Bridon G, DeCamp LM, Kitchen-Goosen SM, Avizonis D, Sheldon RD, Laister RC, Minden MD, Johnson NA, Duchaine TF, Rudoltz MS, Yoo S, Pollak MN, Williams KS, Jones RG. Repression of LKB1 by miR-17~92 Sensitizes MYC-Dependent Lymphoma to Biguanide Treatment. Cell Rep Med. 2020 May 19;1(2):100014. doi: 10.1016/j.xcrm.2020.100014. PMID: 32478334; PMCID: PMC7249503.

7. Bioactivity

Biological target:

IM156 is a biguanide compound and mitochondrial oxidative phosphorylation (OxPhos) inhibitor, with potential antineoplastic activity.

In vitro activity

The biological properties of phenformin and the newly developed biguanide IM156, which are more hydrophobic and therefore potentially more bioavailable to cells than metformin (Figure 1A), were investigated. To test the impact of these biguanides on tumor cell respiration, Myc-dependent mouse lymphoma cells (Eμ-Myc cells) were acutely treated with either metformin, phenformin, or IM156 and assessed changes in the oxygen consumption rate (OCR) using the Seahorse XF96 extracellular flux analyzer. Across a range of concentrations, phenformin and IM156 decreased OCR (Figure 1B), with IM156 exhibiting greater potency than phenformin and metformin at equal concentrations. IM156 was more effective than phenformin at reducing cellular ATP production at equal concentrations, correlating with the effect of IM156 on oxidative phosphorylation (Figure 1C). These data are consistent with IM156 functioning as a more potent inhibitor of mitochondrial respiration than phenformin. IM156 also reduced NADH oxidation in purified complex I in a dose-dependent manner (Figure S1A). To further confirm the specificity of IM156 for complex I, the IM156-mediated inhibition of OCR was assessed in cells expressing NDI1, a yeast NADH dehydrogenase that is resistant to biguanides.28 NDI1 expression rescued the effects of IM156 on cellular respiration, promoting an ~100-fold shift in the IC50 of IM156 (Figure 1E). These data support that IM156 blocks OXPHOS through the inhibition of complex I and does so more potently than phenformin.

Reference: Cell Rep Med. 2020 May 19;1(2):100014. https://pubmed.ncbi.nlm.nih.gov/32478334/.

In vivo activity

In this study, it was investigated how IM156 treatment affects antigen-specific CD8+ T cell differentiation in vivo during acute infection with acute lymphocytic choriomeningitis virus (LCMV) in five- to 6-wk-old female C57BL/6 mice. To examine whether in vivo treatment of IM156 affects the function of memory T cells, splenocytes obtained at day 30 post-infection were re-stimulated ex vivo with the virus-specific peptide GP33-41 for CD8+ T cells and GP66-80 for CD4+ T cells. The percentage and expression levels of TNF-α- and IL-2-producing cells among IFN-γ+CD8+ T cells decreased dose-dependently in the IM156-treated group (Fig. 4A and B). Similar results were observed for IFN-γ+CD4+ T cells in IM156-treated mice (Fig. 4C and D). It has been reported that CD107a represents cytotoxic CD8+ and CD4+ T cell responses to viral and tumor antigen associated with T cell cytolytic potential (16,17,18,19). However, there was no difference in CD107a expression on CD8+ and CD4+ T cells after in vivo treatment with various doses of IM156, indicating that IM156 does not affect the cytotoxicity of T cells (Supplementary Fig. 2). Although the cytotoxic potential was not altered by IM156, the polyfunctionality of CD8+ and CD4+ T cells was significantly decreased after IM156 treatment as shown in Fig. 4, suggesting that IM156 modulates the ability of T cells to produce effector cytokines but not their cytotoxicity after viral infection.

Reference: Immune Netw. 2019 Apr; 19(2): e11. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6494768/

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.