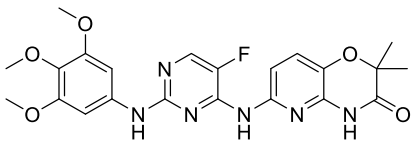
Product data sheet

MedKoo Cat#: 205926 Name: Tamatinib free base CAS#: 841290-80-0 (free base) Chemical Formula: $C_{22}H_{23}FN_6O_5$ Exact Mass: 470.1714 Molecular Weight: 470.45	
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:

Tamatinib, also known as R406, is a potent inhibitor of immunoglobulin E (IgE)- and IgG-mediated activation of Fc receptor signaling (EC(50) for degranulation = 56-64 nM). The primary target for R406 is the spleen tyrosine kinase (Syk). R406 inhibited phosphorylation of Syk substrate linker for activation of T cells in mast cells and B-cell linker protein/SLP65 in B cells. R406 bound to the ATP binding pocket of Syk and inhibited its kinase activity as an ATP-competitive inhibitor (K(i) = 30 nM).

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	13.17	27.99
DMF	0.5	1.06

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.13 mL	10.63 mL	21.26 mL
5 mM	0.43 mL	2.13 mL	4.25 mL
10 mM	0.21 mL	1.06 mL	2.13 mL
50 mM	0.04 mL	0.21 mL	0.43 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. Cho HJ, Yang EJ, Park JT, Kim JR, Kim EC, Jung KJ, Park SC, Lee YS. Identification of SYK inhibitor, R406 as a novel senolytic agent. Aging (Albany NY). 2020 May 7;12(9):8221-8240. doi: 10.18632/aging.103135. Epub 2020 May 7. PMID: 32379705; PMCID: PMC7244031.
2. Sun S, Xue D, Chen Z, Ou-Yang Y, Zhang J, Mai J, Gu J, Lu W, Liu X, Liu W, Sheng L, Lu B, Lin Y, Xing F, Chen Z, Mou Y, Yan G, Zhu W, Sai K. R406 elicits anti-Warburg effect via Syk-dependent and -independent mechanisms to trigger apoptosis in glioma stem cells. Cell Death Dis. 2019 May 1;10(5):358. doi: 10.1038/s41419-019-1587-0. PMID: 31043589; PMCID: PMC6494878.

In vivo study

1. Wang W, Ren S, Lu Y, Chen X, Qu J, Ma X, Deng Q, Hu Z, Jin Y, Zhou Z, Ge W, Zhu Y, Yang N, Li Q, Pu J, Chen G, Ye C, Wang H, Zhao X, Liu Z, Zhu S. Inhibition of Syk promotes chemical reprogramming of fibroblasts via metabolic rewiring and H2 S production. EMBO J. 2021 Jun 1;40(11):e106771. doi: 10.15252/embj.2020106771. Epub 2021 Apr 28. PMID: 33909912; PMCID: PMC8167362.

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2. Nadeem A, Ahmad SF, Al-Harbi NO, Al-Harbi MM, Ibrahim KE, Kundu S, Attia SM, Alanazi WA, AlSharari SD. Inhibition of spleen tyrosine kinase signaling protects against acute lung injury through blockade of NADPH oxidase and IL-17A in neutrophils and γδ T cells respectively in mice. Int Immunopharmacol. 2019 Mar;68:39-47. doi: 10.1016/j.intimp.2018.12.062. Epub 2019 Jan 2. PMID: 30611000.

7. Bioactivity

Biological target:

R406 free base inhibits Syk kinase activity in vitro with an IC50 of 41 nM, and also inhibits Lyn (IC50=63 nM) and Lck (IC50=37 nM).

In vitro activity

Among these, R406, an FDA-approved Syk inhibitor, was found to exhibit higher cytotoxicity in senescent HDFs than in non-senescent cells over the tested range of concentration (from 1 to 20 μM; Figure 1A). In addition, this study further confirmed R406-induced cytotoxicity by Hoechst 33342 staining, because CCK-1-based cell viability assay could reflect cell metabolic activity, which might be influenced by kinase inhibitors. Similar to the CCK-1 assay, the fluorescence levels of senescent HDFs were reduced by R406 in a dose dependent manner (Supplementary Figure 2C). These results demonstrated that R406 has cytotoxicity selectively in senescent fibroblasts in the RS model and, subsequent experiments were performed using R406 concentration of 10 μM.

Reference: Aging (Albany NY). 2020 May 15; 12(9): 8221–8240. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7244031/

In vivo activity

LPS-induced increase in all of these inflammatory parameters was blocked by SYK inhibitor, R406 (Fig. 1A–E). Mice which underwent LPS-induced ALI had higher mortality rate at the end of 5-day period as compared to other groups, i.e. PBS group, SYKinhib group, and LPS + SYKinhib group (Fig. 1F). These findings show that SYK inhibition results in amelioration of LPS-induced ALI which is associated with reduced mortality.

Reference: Int Immunopharmacol. 2019 Mar;68:39-47. https://pubmed.ncbi.nlm.nih.gov/30611000/

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.