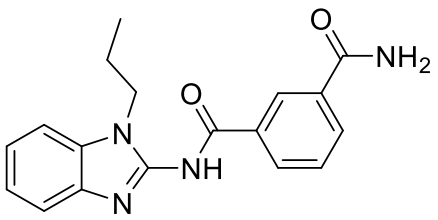
Product data sheet

MedKoo Cat#: 561836 Name: Takinib CAS#: 1111556-37-6 Chemical Formula: $C_{18}H_{18}N_4O_2$ Exact Mass: 322.143 Molecular Weight: 322.36	
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:
Takinib is a selective TAK1 inhibitor that induces apoptosis following TNF-α stimulation in cell models of rheumatoid arthritis and metastatic breast cancer. Takinib is an inhibitor of autophosphorylated and non-phosphorylated TAK1 that binds within the ATP-binding pocket and inhibits by slowing down the rate-limiting step of TAK1 activation.

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	93.06

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.10 mL	15.51 mL	31.02 mL
5 mM	0.62 mL	3.10 mL	6.20 mL
10 mM	0.31 mL	1.55 mL	3.10 mL
50 mM	0.06 mL	0.31 mL	0.62 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. Totzke J, Gurbani D, Raphemot R, Hughes PF, Bodoor K, Carlson DA, Loiselle DR, Bera AK, Eibschutz LS, Perkins MM, Eubanks AL, Campbell PL, Fox DA, Westover KD, Haystead TAJ, Derbyshire ER. Takinib, a Selective TAK1 Inhibitor, Broadens the Therapeutic Efficacy of TNF-α Inhibition for Cancer and Autoimmune Disease. Cell Chem Biol. 2017 Aug 17;24(8):1029-1039.e7. doi: 10.1016/j.chembiol.2017.07.011. PMID: 28820959; PMCID: PMC5576570.

In vivo study

1. Scarneo SA, Eibschutz LS, Bendele PJ, Yang KW, Totzke J, Hughes P, Fox DA, Haystead TAJ. Pharmacological inhibition of TAK1, with the selective inhibitor takinib, alleviates clinical manifestation of arthritis in CIA mice. Arthritis Res Ther. 2019 Dec 17;21(1):292. doi: 10.1186/s13075-019-2073-x. PMID: 31847895; PMCID: PMC6918687.

7. Bioactivity
Biological target:

Takinib is a potent and selective TAK1 inhibitor with an IC50 of 9.5 nM.

In vitro activity

Product data sheet

MDA-MB-231 cells were serum-starved for 3h and pre-treated with 10μM Takinib for 2h. Stimulation of cells with TNFα was performed over a time-course of 60min and the phosphorylation status of IKK, p38, and p65 was determined via Western Blot (Fig. 5B). IKK and p65 are maximally phosphorylated at 15 minutes, which indicate activation of the NFkB pathway, while p38 phosphorylation peaks at 30 minutes. Takinib reduced phosphorylation of significantly but did not influence total protein levels. Dose-dependency studies were performed in Hela cells following 15 minutes of TNFα stimulation. Western Blot analysis demonstrated that Takinib inhibits phosphorylation of IKK, MAPK 8/9, and cJun in a dose-dependent manner (Fig. 5C). Additionally, we investigated cellular TAK1 autophosphorylation following 15min of TNFα stimulation. Thr184 phosphorylation was significantly reduced at low μM concentrations (Fig. S3A).

Reference: Cell Chem Biol. 2017 Aug 17;24(8):1029-1039.e7. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/28820959/

In vivo activity

Takinib has an ability to reduce the clinical score in the CIA mouse model of rheumatoid arthritis (RA) ($p < 0.001$). TAK1 inhibition reduced inflammation ($p < 0.01$), cartilage damage ($p < 0.01$), pannus, bone resorption, and periosteal bone formation and periosteal bone width in all joints of treated mice compared to vehicle treated. Significant reduction of inflammation ($p < 0.004$) and cartilage damage ($p < 0.004$) were observed in the knees of diseased treated animals, with moderate reduction seen in the forepaws and hind paws. Furthermore, the pharmacokinetics of takinib show rapid plasma clearance ($t½ = 21$ min). In stimulated RA-FLS cells, takinib reduced GROα, G-CSF, and ICAM-1 pro-inflammatory cytokine signaling.

Reference: Arthritis Res Ther. 2019 Dec 17;21(1):292. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/31847895/

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.