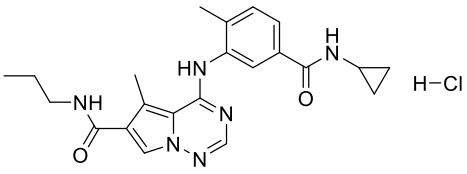
Product data sheet

MedKoo Cat#: 522406 Name: BMS-582949 HCl CAS#: 912806-16-7 (HCl) Chemical Formula: $C_{22}H_{27}ClN_6O_2$ Exact Mass: 406.21172 Molecular Weight: 442.948	
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:
BMS-582949 is a potent and selective P38 mitogen-activated protein kinase (P38 MAPK) inhibitor. BMS-582949 is currently under Phase II clinical trials for the treatment of inflammatory diseases. One clinical study showed that, in stable atherosclerosis, 12 weeks of treatment with BMS-582949 did not reduce arterial inflammation or hs-CRP compared to placebo, whereas intensification of statin therapy significantly decreased arterial inflammation. p38α MAP kinase plays a crucial role in regulating the biosynthesis of many inflammatory cytokines including TNFα and IL-1β.

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	25.0	56.44

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.26 mL	11.29 mL	22.58 mL
5 mM	0.45 mL	2.26 mL	4.52 mL
10 mM	0.23 mL	1.13 mL	2.26 mL
50 mM	0.05 mL	0.23 mL	0.45 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. Freebern WJ, Bigwarfe TJ, Price KD, Haggerty HG. Methods: implementation of in vitro and ex vivo phagocytosis and respiratory burst function assessments in safety testing. J Immunotoxicol. 2013 Jan-Mar;10(1):106-17. doi: 10.3109/1547691X.2012.736427. Epub 2012 Nov 23. PMID: 23173903.

In vivo study

1. Liu C, Lin J, Hynes J, Wu H, Wrobleski ST, Lin S, Dhar TG, Vrudhula VM, Sun JH, Chao S, Zhao R, Wang B, Chen BC, Everlof G, Gesenberg C, Zhang H, Marathe PH, McIntyre KW, Taylor TL, Gillooly K, Shuster DJ, McKinnon M, Dodd JH, Barrish JC, Schieven GL, Leftheris K. Discovery of ((4-(5-(Cyclopropylcarbamoyl)-2-methylphenylamino)-5-methylpyrrolo[1,2-f][1,2,4]triazine-6-carbonyl)(propyl)carbamoyloxy)methyl-2-(4-(phosphonooxy)phenyl)acetate (BMS-751324), a Clinical Prodrug of p38α MAP Kinase Inhibitor. J Med Chem. 2015 Oct 8;58(19):7775-84. doi: 10.1021/acs.jmedchem.5b00839. Epub 2015 Sep 22. PMID: 26359680.

7. Bioactivity
Biological target:

Product data sheet

BMS-582949 hydrochloride is an orally active and highly selective p38α MAPK inhibitor, with an IC50 of 13 nM.

In vitro activity

An investigative study was conducted to evaluate the effects of BMS-582949 in rat and monkey neutrophils and monocytes in vitro. BMS-582949 inhibited phagocytosis in monkey and rat neutrophils in a dose-dependent manner (Figure 5). Phagocytosis function was significantly ($p \leqslant 0.05$) decreased in rat and monkey neutrophils at 0.5 µM (0.2 µg/ml), 5 µM (2.1 µg/ml), and 50 µM (21 µg/ml). At 5 and 50 µM the median percent inhibitions were higher for monkeys (37 and 44%, respectively) than rats (16 and 27%, respectively). The incidence of $\geqslant$ 30% inhibition was also higher in monkeys (Table 3). The species differences in median percent inhibition and incidence of $\geqslant$ 30% inhibition are reflected in the higher IC30 values for rat (62 µM, 25 µg/ml) than monkey (23.2 µM, 9.4 µg/ml). Regardless of the group median differences between monkey and rat, there are several individual incidences of $\geqslant$ 30% inhibition of neutrophil phagocytosis observed in both monkey and rat (Table 3) at 5 µM (2.1 µg/ml) BMS-582949, which is 0.1 – 10× the Cmax values achieved in animals with infections. There were no BMS-582949-related effects on monocyte phagocytosis function demonstrated in monkeys or rats.

Reference: J Immunotoxicol. 2013 Jan-Mar;10(1):106-17. https://www.tandfonline.com/doi/full/10.3109/1547691X.2012.736427

In vivo activity

Inhibitor 7k (BMS-582949) is slightly less active than 1a in the p38α enzymatic assay but displays a superior pharmacokinetic profile and, as such, was more effective in both the acute murine model of inflammation and pseudoestablished rat AA model.

Reference: J Med Chem. 2015 Oct 8;58(19):7775-84. https://pubmed.ncbi.nlm.nih.gov/20804198/

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.