BMS-582949

Cat. No.: HY-14305

CAS No.: 623152-17-0

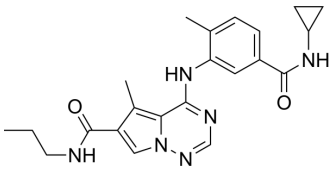
Molecular Formula: $C_{22}H_{26}N_6O_2$

Molecular Weight: 406.48

Target: p38 MAPK

Pathway: MAPK/ERK Pathway

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

BMS-582949 (compound 7k) is an orally active and highly selective p38α MAP kinase inhibitor, with IC_{50} values of 13 nM for p38α, and 50 nM for cellular TNFα. BMS-582949 can be used for research on rheumatoid arthritis[1].

IC_{50} & Target

p38α
13 nM (IC_{50})

In Vivo

BMS-582949 (5 mg/kg, p.o., 90 min) reduces the LPS induced TNFα production significantly in murine models of acute inflammation from BALB/c female mice[1].

BMS-582949 (0.3-100 mg/kg, p.o., q.d/b.i.d) reduces paw swelling significantly[1].

BMS-582949 intravenous injection (i.v.) dissolution protocol uses 25% NMP, 33% PEG 400, 9% PG, and 33% water as a vehicle [1].

BMS-582949 oral gavage (p.o.) dissolution protocol uses PEG 400 as a vehicle[1].

Pharmacokinetic Properties of Compound 7k in Mice and Rats[1]

Compound 7k [illegible][1]

	mouse	rat
$\%F_{po}$	90	60
C_{max}(μM)	15.3	7.0
T_{max}(h)	1.0	1.5
$T_{1/2}$(h)	2.6	4.0
MRT (h)	3.3	3.4
CL (mL/min/kg)	4.4	5.4

V_{ss}(L/kg)	0.9	1.1
$AUC_{0\text{-}8\ h}$(μM•h)	75.5	
$AUC_{0\text{-}24\ h}$(μM•h)		45.4

In Vitro Profile of 7k[1]

□□□□□□[1]

profiling assays	results
liver microsome metabolic rate (nmol/min/mg)	mouse: 0.011 rat: 0.008 human: 0.013
hepatocyte metabolic rate (nmol/min/million cells)	mouse: 0.006 rat: 0.015 human: 0.015
P450 IC_{50}(μM)	>40 for 1A2, 2C9 2C19, and 2D6 18-40 for 3A4
Caco-2 permeability (nm/s)	121-134
serum protein binding (%)	mouse: 86.3 rat: 89.7 human: 81.5
Ames	negative in T98 and T100±S9 activation
SOS chromotest	negative
HHA IC_{50}(μM)	>138
hERG inhibition	16% at 30 μM
kinase selectivity	>2000 fold over 57 diverse kinase 450 fold over Jnk2 190 fold over Raf 5 fold over p38α

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	murine models of acute inflammation from BALB/c female mice[1]
Dosage:	5 mg/kg
Administration:	Oral gavage (p.o.), detection content at 90 min after LPS injection
Result:	Reduced the TNFα production by 89% at 2 h, by 78% at 6 h before the LPS challenge.

Animal Model:	Rat adjuvant arthritis (rat AA) models from Male Lewis rats[1]
Dosage:	1, 10, 100 mg/kg, once daily (q.d)
Administration:	Oral gavage (p.o.)
Result:	Reduced paw swelling with dose-dependent, with efficacy observed at doses of 10 and 100 mg/kg.

Animal Model:	Rat adjuvant arthritis (rat AA) models from Male Lewis rats[1]
Dosage:	0-5 mg/kg, b.i.d
Administration:	Oral gavage (p.o.)
Result:	Improved efficacy markedly of reduction in paw swelling at doses of 1 and 5 mg/kg. Reduced paw swelling significantly at doses as low as 0.3 mg/kg.

CUSTOMER VALIDATION

- Oncol Res. 2021 Feb 11.

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REFERENCES

[1]. Liu C, et al. Discovery of 4-(5-(cyclopropylcarbamoyl)-2-methylphenylamino)-5-methyl-N-propylpyrrolo[1,2-f][1,2,4]triazine-6-carboxamide (BMS-582949), a clinical p38α MAP kinase inhibitor for the treatment of inflammatory diseases. J Med Chem. 2010 Sep 23;53(18):6629-39.

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