SAR-20347

Cat. No.: HY-100895

CAS No.: 1450881-55-6

Molecular Formula: $C_{21}H_{18}ClFN_4O_4$

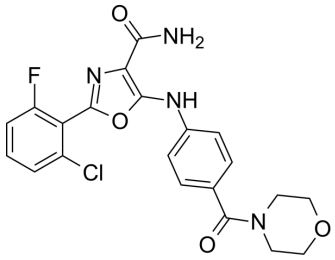
Molecular Weight: 444.84

Target: JAK

Pathway: Epigenetics; JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Stem Cell/Wnt

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (224.80 mM; Need ultrasonic and warming)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2480 mL	11.2400 mL	22.4800 mL
	5 mM	0.4496 mL	2.2480 mL	4.4960 mL
	10 mM	0.2248 mL	1.1240 mL	2.2480 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.62 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.62 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SAR-20347 is an inhibitor of TYK2, JAK1, JAK2 and JAK3 with IC_{50}s of 0.6, 23, 26 and 41 nM, respectively.

IC_{50} & Target

Tyk2	JAK1	JAK2	JAK3
0.6 nM (IC_{50})	23 nM (IC_{50})	26 nM (IC_{50})	41 nM (IC_{50})

In Vitro

When NK-92 cells are stimulated with IL-12, SAR-20347 potently inhibits IL-12-mediated STAT4 phosphorylation, a TYK2-dependent event, with an IC_{50} of 126 nM. SAR-20347 demonstrates a selectivity of TYK2>JAK1>JAK2>JAK3. Cells without IL-12 in the culture media have no measureable IFN-γ, while cells incubated with IL-12 and SAR-20347 demonstrate dose-dependent inhibition of IFN-γ production. SAR-20347 dose-dependently inhibits the production of secreted embryonic alkaline phosphatase (SEAP) with greatest inhibition occurring with 5 μM of SAR-20347 in these experiments[1].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	60 mg/kg SAR-20347 inhibits the production of IFN-γ in the serum by 91% compare to vehicle-treated animals, demonstrating that SAR-20347 can inhibit TYK2 signaling in vivo. SAR-20347 treatment significantly reduces IL-17 production as measured by average signal intensity, consistent with the gene expression analysis[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Kinases are prepared in Base Reaction Buffer (20 mM Hepes pH 7.5, 10 mM $MgCl_2$, 1 mM EGTA, 0.02% Brij35, 0.02 mg/mL BSA, 0.1 mM Na_3VO_4, 2 mM DTT, 1% DMSO) and substrate is added with 1.5 mM $CaCl_2$, 16 μg/mL Calmodulin, and 2 mM $MnCl_2$. Varying concentrations of SAR-20347 in DMSO are added to the kinase reaction along with 10 μM ^{33}P-ATP (activity 0.01 μCi/μL final) for IC_{50} determination[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	Cells are plated in a 96-well v-bottom plate in starvation medium, incubated with SAR-20347 (0.5% DMSO) for 20 minutes at 37°C, 5% CO_2, and stimulated with individual cytokines. P-STAT levels are measured in duplicate using MSD plates following the manufacturer's instructions (MSD). The IC_{50} is determined by subtracting background (no cytokine) and relative to DMSO/cytokine control[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Female 7 to 9 week old C57BL/6 mice are used. Mice are administered vehicle or 50 mg/kg SAR-20347 by oral gavage 30 minutes prior to application of 62.5 mg 5% imiquimod cream or control cream. Another dose of vehicle or 50 mg/kg SAR-20347 is given 5.5 hours following the first dose. This treatment is repeated for 5 days and on day 3 and 4, animals are injected with 100 uL saline to prevent dehydration. Each day, the mice are assessed by the same researcher for redness. On the 6th day, the animals are euthanized and photographs are taken[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Res. 2019 Mar;29(3):193-205.

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REFERENCES

[1]. Works MG, et al. Inhibition of TYK2 and JAK1 ameliorates imiquimod-induced psoriasis-like dermatitis by inhibiting IL-22 and the IL-23/IL-17 axis. J Immunol. 2014 Oct 1;193(7):3278-87.

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