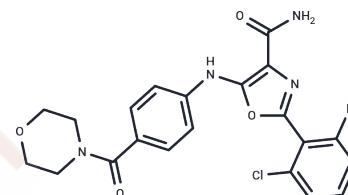


SAR-20347

Chemical Properties

CAS No. : 1450881-55-6
 Formula: C₂₁H₁₈ClFN₄O₄
 Molecular Weight: 444.84
 Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
 Actual storage temperature shall be subject to the COA.



Biological Description

Description	SAR-20347 is an inhibitor of TYK2 and JAK1/2/3, with IC ₅₀ values of 0.6 nM, 23 nM, 26 nM, and 41 nM, respectively.
Targets(IC ₅₀)	JAK, Tyrosine Kinases
In vitro	SAR-20347 effectively inhibits IL-12-mediated STAT4 phosphorylation (TYK2-dependent, IC ₅₀ : 126 nM) when NK-92 cells are stimulated with IL-12. In the culture media, cells without IL-12 have no measurable IFN- γ , while cells incubated with IL-12 and SAR-20347 demonstrate dose-dependent inhibition of IFN- γ production. SAR-20347 (maximum effect: 5 μ M) dose-dependently inhibits the production of secreted embryonic alkaline phosphatase (SEAP).
In vivo	Compared to vehicle-treated animals, SAR-20347 (60 mg/kg) inhibits the production of IFN- γ in the serum by 91%, demonstrating that SAR-20347 can inhibit TYK2 signaling in vivo. SAR-20347 markedly reduces IL-17 production as measured by average signal intensity, consistent with the gene expression analysis.
Kinase Assay	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 ₃ VO ₄ , 2 mM DTT, 1% DMSO) and substrate is added with 1.5 mM CaCl ₂ , 16 μ g/mL Calmodulin, and 2 mM MnCl ₂ . Varying concentrations of SAR-20347 in DMSO are added to the kinase reaction along with 10 μ M 33P-ATP (activity 0.01 μ Ci/ μ L final) for IC ₅₀ determination[1].
Cell Research	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)[1].
Animal Research	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 μ L saline to prevent dehydration. On the 6th day, the animals are euthanized and photographs are taken[1].

Solubility Information

A DRUG SCREENING EXPERT

Solubility	DMSO: 55 mg/mL (123.64 mM), Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (4.5 mM), Sonication is recommended. <i>Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.</i>

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.248 mL	11.240 mL	22.480 mL
5 mM	0.4496 mL	2.248 mL	4.496 mL
10 mM	0.2248 mL	1.124 mL	2.248 mL
50 mM	0.045 mL	0.2248 mL	0.4496 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

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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