AX-024

Cat. No.: HY-107390

CAS No.: 1370544-73-2

Molecular Formula: $C_{21}H_{22}FNO_2$

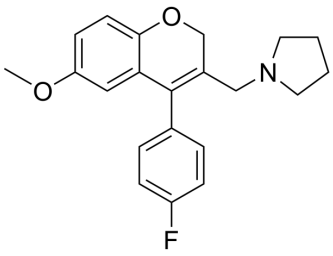
Molecular Weight: 339.4

Target: TNF Receptor; Interleukin Related; IFNAR

Pathway: Apoptosis; Immunology/Inflammation

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

Ethanol : 100 mg/mL (294.64 mM; Need ultrasonic)

DMSO : 35 mg/mL (103.12 mM; Need ultrasonic and warming)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.9464 mL	14.7319 mL	29.4638 mL
5 mM	0.5893 mL	2.9464 mL	5.8928 mL
10 mM	0.2946 mL	1.4732 mL	2.9464 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 (7.37 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (7.37 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.37 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AX-024 is an orally available, first-in-class inhibitor of the TCR-Nck interaction that selectively inhibits TCR-triggered T cell activation with an IC_{50} ~1 nM. AX-024 modulates cell signaling by targeting SH3 domains. AX-024 has low-acute toxicity and high potency and selectivity, and strongly inhibit the production of IL-6, TNF-α, IFN-γ, IL-10 and IL-17A.

IC_{50} & Target	IL-6	IL-10	IL-17A

In Vitro	AX-024 is >10,000-fold more potent than the AX-000 hit in terms of inhibition of TCR-triggered T cell proliferation. The IC_{50} of AX-024 in this assay is 1 nM, although it shows inhibitory effects at a concentration of 1 pM or less. AX-024 is also a much more potent inhibitor of cytokine release by human peripheral blood mononuclear cells stimulated with anti-CD3 than AX-000, strongly hindering interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), interferon-γ (IFN-γ), IL-10, and IL-17A production at a concentration of 10 nM. In $CD8^+$ T cells of OT1 TCR transgenic ($OT1^{Tg}$) mice bearing wild-type (WT) AX-024 strongly inhibits T cell proliferation at a concentration of 0.1 nM when $OT1^{Tg}$ T cells are WT for the PRS mutation. Coimmunoprecipitation experiments in these cells show that Nck recruitment to the TCR is induced upon stimulation in the absence of drug but is inhibited in the presence of AX-024 in a dose-dependent manner at concentrations starting from 1 nM [1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	AX-024-treated group presents less scales and reduces skin thickening compare to the vehicle group. AX-024 significantly reduces thickening of both skin layers, but more effectively of the dermis, which rather resembles that of mice treated with a control cream lacking imiquimod (IMQ). AX-024 significantly diminishes the number of airway inflammatory cells in both assays. Mice receiving AX-024 rapidly recovers from neurological impairment and weight loss, becoming symptom-free by day 30, unlike mice that receives the vehicle, in which ataxia and loss of the righting reflex persist[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Spleen B cells from C57BL/6 mice are labeled with Cell Trace Violet and incubated for 72 hours with either anti-IgM (10 mg/mL) or anti-CD40 (5 mg/mL), supplemented with IL-4 (5 ng/mL) or LPS (2.5 mg/mL) in the presence of different concentrations of AX-024. Proliferation is calculated according to the total number of cell divisions[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Eight-week-old CD-1 mice are injected intraperitoneally with different amounts of the AX-024 dissolved in 0.5 mL of saline. All animals are observed clinically for the appearance of macroscopically visible adverse reactions twice daily over 14 days, as well as immediately after AX-024 administration. A necropsy is carried out on each animal on day 14, and the abdominal, thoracic, and cranial cavities are examined in situ, together with their associated organs[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Life Sci. 2020 May 1;248:117456.

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REFERENCES

[1]. Borroto A, et al. First-in-class inhibitor of the T cell receptor for the treatment of autoimmune diseases. Sci Transl Med. 2016 Dec 21;8(370):370ra184.

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