Ivarmacitinib

Cat. No.: HY-112724

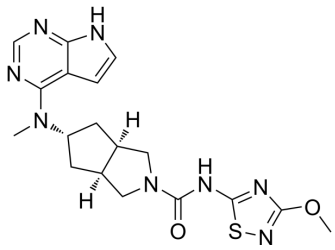
CAS No.: 1445987-21-2

Molecular Formula: $C_{18}H_{22}N_8O_2S$

Molecular Weight: 414.48

Target: JAK; Apoptosis

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



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 : 31.25 mg/mL (75.40 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4127 mL	12.0633 mL	24.1266 mL
	5 mM	0.4825 mL	2.4127 mL	4.8253 mL
	10 mM	0.2413 mL	1.2063 mL	2.4127 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: ≥ 2.08 mg/mL (5.02 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.02 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.02 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Ivarmacitinib (SHR0302) is a potent and orally active all members of the JAK family inhibitor, particularly JAK1. The selectivity of Ivarmacitinib for JAK1 is >10-fold for JAK2, 77-fold for JAK3, 420-fold for Tyk2. Ivarmacitinib inhibits JAK1-STAT3 phosphorylation and induces the apoptosis of hepatic stellate cells. Ivarmacitinib has anti-proliferative and anti-inflammatory effects[1][2].

IC_{50} & Target	JAK1	JAK2	JAK3	Tyk2

In Vitro

Ivarmacitinib (SHR0302; 1 nM-10 μM; 48 hours; HSCs) treatment displays an inhibitory effect on the proliferation of HSCs in a concentration-dependent manner[2].
Ivarmacitinib (1 nM-10 μM) exerts an inhibitory effect on the activation, proliferation and migration of HSCs[2].
Ivarmacitinib (1 nM-10 μM; 48 hours; HSCs) treatment induces the apoptosis of HSCs[2].
Ivarmacitinib (1 nM-10 μM; 48 hours; HSCs) treatment significantly increases the activation of caspase-3 and Bax in HSCs, and decreases the expression of Bcl-2. SHR0302 also inhibits the activation of Akt signaling pathway[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[2]

Cell Line:	Hepatic stellate cells (HSCs)
Concentration:	1 nM, 10 nM, 100 nM, 1μM, 10 μM
Incubation Time:	48 hours
Result:	Displayed an inhibitory effect on the proliferation of HSCs, and that inhibition ocurred in a concentration-dependent manner.

Apoptosis Analysis[2]

Cell Line:	Hepatic stellate cells (HSCs)
Concentration:	1 nM, 10 nM, 100 nM, 1μM, 10 μM
Incubation Time:	48 hours
Result:	Induced the apoptosis of HSCs.

Western Blot Analysis[2]

Cell Line:	Hepatic stellate cells (HSCs)
Concentration:	1 nM, 10 nM, 100 nM, 1μM, 10 μM
Incubation Time:	48 hours
Result:	Significantly increased the activation of caspase-3 and Bax in HSCs, and decreased the expression of Bcl-2. Also inhibited the activation of Akt signaling pathway.

In Vivo

Ivarmacitinib (SHR0302; 0.3-3.0 mg/kg; intragastric administration; twice a day; for 14 days; male Sprague-Dawley (SD) rats) treatment suppresses the severity of AA rats by attenuating the arthritis index, arthritis global assessment and paw swelling degree, and alleviated histopathology of spleen and joint of AA rats[1].
Ivarmacitinib can inhibit the proliferation of T, B and fibroblast-like synoviocytes (FLS), and down-regulates cytokines TNF-α, IL-1β, IL-17 and antibody IgG1, IgG2a levels, and suppresses the proportion of Th17 and total B, and inhibits JAK1-STAT3 phosphorylation[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male Sprague-Dawley (SD) rats (150-180 g) injected with complete Freund's adjuvant (CFA) [1]
Dosage:	0.3 mg/kg,1.0 mg/kg, 3.0 mg/kg
Administration:	Intragastric administration; twice a day; for 14 days
Result:	Suppressed the severity of adjuvant-induced arthritis (AA) rats by attenuating the arthritis index, arthritis global assessment and paw swelling degree, and alleviated histopathology

	of spleen and joint of AA rats.

REFERENCES

[1]. Huaxun Wu, et al. JAK1-STAT3 Blockade by JAK Inhibitor SHR0302 Attenuates Inflammatory Responses of Adjuvant-Induced Arthritis Rats and Decreases Th17 and Total B Cells. Joint Bone Spine. 2016 Oct;83(5):525-32.

[2]. Yuan-Jing Gu, et al. Targeted Blockade of JAK/STAT3 Signaling Inhibits Proliferation, Migration and Collagen Production as Well as Inducing the Apoptosis of Hepatic Stellate Cells. Int J Mol Med. 2016 Sep;38(3):903-11.

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