Peficitinib

Cat. No.: HY-19568

CAS No.: 944118-01-8

Molecular Formula: $C_{18}H_{22}N_4O_2$

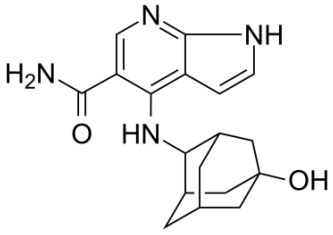
Molecular Weight: 326.39

Target: JAK

Pathway: Epigenetics; JAK/STAT Signaling; Stem Cell/Wnt

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 60 mg/mL (183.83 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.0638 mL	15.3191 mL	30.6382 mL
5 mM	0.6128 mL	3.0638 mL	6.1276 mL
10 mM	0.3064 mL	1.5319 mL	3.0638 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 (7.66 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (7.66 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Peficitinib is an oral JAK inhibitor, with IC_{50}s of 3.9, 5.0, 0.7 and 4.8 nM for JAK1, JAK2, JAK3 and Tyk2, respectively.

IC_{50} & Target

JAK3	JAK1	Tyk2	JAK2
0.7 nM (IC_{50})	3.9 nM (IC_{50})	4.8 nM (IC_{50})	5 nM (IC_{50})

In Vitro

Peficitinib is an oral JAK inhibitor, with IC_{50}s of 3.9, 5.0, 0.7 and 4.8 nM for JAK1, JAK2, JAK3 and Tyk2, respectively.
Peficitinib inhibits IL-2-induced T cell proliferation with an IC_{50} of 10 nM. Peficitinib also suppresses the IL-2-induced STAT5 phosphorylation in rat and human whole blood, with mean IC_{50}s of 124 nM and 127 nM, respectively[1].

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

In Vivo	Peficitinib (20 mg/kg, p.o.) suppresses IL-2-induced STAT5 phosphorylation by 78% in the rat model of adjuvant-induced arthritis (AIA). Peficitinib potently inhibits the increase in paw volume (≥1 mg/kg) with an ED_{50} of 2.7 mg/kg, significantly reduces the bone destruction score (≥10 mg/kg) and almost fully ameliorates both paw swelling and bone destruction scores (30 mg/kg)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Human JAK1, JAK2, JAK3, TYK2-domains assays performed using streptavidin-coated 96-well plates. Reaction mixture contained 15 mM Tris-HCl (pH 7.5), 0.01% Tween 20, 2 mM dithiothreitol, 10 mM $MgCl_2$, 250 nM Biotin-Lyn-Substrate-2 (for JAK1, 2 and 3) or Biotin-IRS1-Substrate (for TYK2), and ATP (at final concentrations of 200 μM [JAK1], 10 μM [JAK2], 8 μM [JAK3], and 4 μM [TYK2]). Peficitinib or tofacitinib is dissolved in DMSO. The reaction is initiated by adding the kinase domain, followed by incubation at room temperature for 1 h. Kinase activity is measured as the rate of phosphorylation of Biotin-Lyn-Substrate-2 or Biotin-IRS-Substrate using HRP-conjugated anti-phosphotyrosine antibody (HRP-PY-20) using a phosphotyrosine-specific ELISA. TYK2 kinase assay of Peficitinib is performed with the ATP concentration of 10 μM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	Splenocytes from male Lewis rats are suspended in RPMI1640 supplemented with 10% fetal bovine serum and 50 μM 2-mercaptoethanol at a density of 1.5×10^6 cells/mL. Rat splenocytes are cultured with Concanavalin A for 24 h at 37°C to induce IL-2 receptor expression. Splenocytes are then incubated with IL-2 and Peficitinib or tofacitinib at designated concentrations in 96-well tissue culture plates. After 3-day incubation, alamarBlue® is added to each of the test wells, followed by 4-6 h incubation. Fluorescence intensity is measured at an excitation wavelength of 545 nm and an emission wavelength of 590 nm. All experiments are performed in triplicate, and experiments are performed either four times or once for assays using Peficitinib or tofacitinib, respectively. For each individual, wells cultured with cells and medium alone are prepared for the blanks, and IL-2 stimulated cells without JAK inhibitors are prepared for the controls. To calculate the % inhibition of JAK inhibitors, blanks and controls are designated as 100% and 0% inhibition, respectively[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Rats[1] Seven-weeks-old female Lewis rats are used for the adjuvant-induced arthritis (AIA) model. Body weight and left hind paw volume of each rat are measured (MK-101PR volume meter), and the values are used to assign animals to one of six groups (n = 10). Arthritis is induced on day 0 in five of these groups by injecting a suspension of Mycobacterium tuberculosis H37 RA strain (0.5 mg/rat) in liquid paraffin into the right hind foot pad. The remaining group is not injected with adjuvant (normal group, n = 10). For the oral administration regimen, four of the adjuvant-injected groups receive Peficitinib (1, 3, 10, and 30 mg/kg) dissolved in 0.5% methylcellulose (MC) once daily. Rats in the normal and control groups receive 0.5% MC alone[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Talanta. 2020 Feb 1;208:120450.
- Cells. 2019 Jun 9;8(6). pii: E561.
- Cancer Manag Res. 2018 Dec 28;11:389-399.

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REFERENCES

[1]. Ito M, et al. A novel JAK inhibitor, peficitinib, demonstrates potent efficacy in a rat adjuvant-induced arthritis model. J Pharmacol Sci. 2017 Jan;133(1):25-33.

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