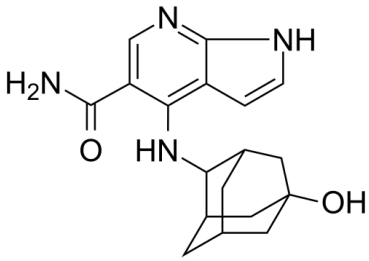
Data Sheet

Product Name:	Peficitinib
Cat. No.:	CS-5393
CAS No.:	944118-01-8
Molecular Formula:	C18H22N4O2
Molecular Weight:	326.39
Target:	JAK
Pathway:	Epigenetics; JAK/STAT Signaling; Stem Cell/Wnt
Solubility:	DMSO : ≥ 60 mg/mL (183.83 mM)



BIOLOGICAL ACTIVITY:

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. IC50 & Target: IC50: 3.9 nM (JAK1), 5.0 nM (JAK2), 0.7 nM (JAK3), 4.8 nM (Tyk2)[1] **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]. **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].

PROTOCOL (Extracted from published papers and Only for reference)

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].

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].

Animal Administration: Peficitinib is dissolved in 0.5% methylcellulose[1].[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].

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.

CAIndexNames:

1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[(5-hydroxytricyclo[3.3.1.13,7]dec-2-yl)amino]-, stereoisomer

SMILES:

O[C@](C[C@@H]1C[C@H]2C3)(C2)C[C@@H]3[C@H]1NC4=C5C(NC=C5)=NC=C4C(N)=O

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