Web: www.taiclone.com
Tel: +886-2-2735-9682
Email: order@taiclone.com

Pacritinib

Catalog No: tcsc1741

Available Sizes

Size: 5mg

Size: 10mg

Size: 50mg

Size: 100mg

Specifications

CAS No:
937272-79-2

Formula:
$C_{28}H_{32}N_4O_3$

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

Target:
FLT3;JAK;JAK;JAK

Purity / Grade:
>98%

Solubility:
DMSO : 5.4 mg/mL (11.43 mM; Need ultrasonic and warming)

Alternative Names:
SB1518

Observed Molecular Weight:
472.58

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Product Description

Pacritinib is a potent inhibitor of both wild-type **JAK2** (IC_{50}=23 nM) and **JAK2^{V617F}** mutant (IC_{50}=19 nM). Pacritinib also inhibits **FLT3** (IC_{50}=22 nM) and its mutant **FLT3^{D835Y}** (IC_{50}=6 nM).

IC50 & Target: IC50: 6 nM ($FLT3^{D835Y}$), 22 nM ($FLT3^{wt}$), 19 nM ($JAK2^{V617F}$), 23 nM ($JAK2^{wt}$)[1]

In Vitro: Relative to JAK2, Pacritinib (SB1518) is two-fold less potent against TYK2 (IC_{50}=50 nM), 23-fold less potent against JAK3 (IC_{50}=520 nM) and 56-fold less potent against JAK1 (IC_{50}=1280 nM). The rest of the evaluated kinases show m). Pacritinib inhibits MV4-11 and MOLM-13 cells (both of which are cell lines derived from human acute myeloid leukemias driven by an FLT3 ITD mutation) with IC_{50} of 47 and 67 nM, respectively. Pacritinib inhibits Karpas 1106P and Ba/F3-$JAK2^{V617F}$ cells (which are cell lines dependent on JAK2 signaling) with IC_{50} of 348 and 160 nM, respectively[1]. FLT3-ITD harboring MV4-11 cells are treated for 3 h with different concentrations of Pacritinib (SB1518) and pFLT3, pSTAT5 and pERK1/2 levels are quantified. Pacritinib leads to a dose-dependent decrease of pFLT3, pSTAT5, pERK1/2 and pAkt with IC_{50} of 80, 40, 33 and 29 nM, respectively. The IC_{50} on auto-phosphorylation of FLT3-wt in RS4;11 is four-fold higher (IC_{50}=600 nM) compare with FLT3-ITD in MV4-11 and MOLM-13 cells. However, STAT5 inhibition is detected at much lower concentrations of Pacritinib (IC_{50}=8 nM)[2].

In Vivo: For evaluation of efficacy in the Ba/F3-$JAK2^{V617F}$ engraftment model, mice are treated with Pacritinib (SB1518) at doses of 50 or 150 mg/kg p.o. q.d. for 13 days, with drug dosing starting 4 days after cell inoculation. At study termination, the vehicle control mice exhibit splenomegaly and hepatomegaly (~7- and 1.3-fold, respectively), reminiscent of the symptoms found in patients with symptomatic myelofibrosis. SB1518 treatment at 150 mg/kg p.o. q.d. significantly ameliorates all these symptoms, with 60% (±9%) normalization of spleen weight and 92% (±5%) normalization of liver weight and is well tolerated without significant weight loss or any hematological toxicities, including thrombocytopenia and anemia[1]. In rats, Pacritinib (SB1518) shows moderately fast absorption (t_{max}=4 h), with a peak concentration of 114 ng/mL, AUC of 599 ng•h/mL, and a terminal half-life of ~6 h following a single oral dose of 10 mg/kg. In dogs, Pacritinib (SB1518) is rapidly absorbed (t_{max}=2.0 h), with a peak concentration of ~12 ng/mL, AUC of 53 ng•h/mL, and a terminal half-life of 3.4 h following a single oral dose of 3 mg/kg[3].