

# 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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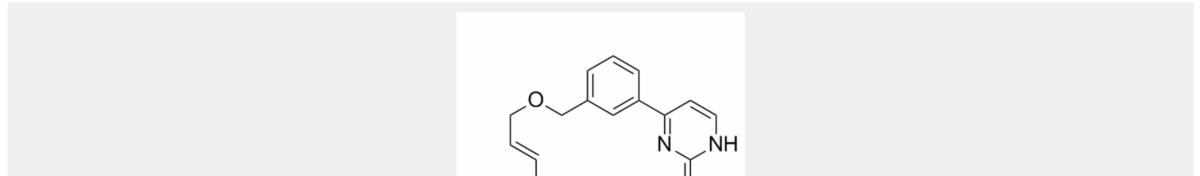
# **Product Description**

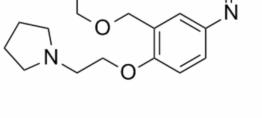
Pacritinib is a potent inhibitor of both wild-type JAK2 (IC<sub>50</sub>=23 nM) and JAK2<sup>V617F</sup> mutant (IC<sub>50</sub>=19 nM). Pacritinib also inhibits FLT3 (IC<sub>50</sub>=22 nM) and its mutant FLT3<sup>D835Y</sup> (IC<sub>50</sub>=6 nM).

IC50 & Target: IC50: 6 nM (FLT3<sup>D835Y</sup>), 22 nM (FLT3<sup>wt</sup>), 19 nM (JAK2<sup>V617F</sup>), 23 nM (JAK2<sup>wt</sup>)<sup>[1]</sup>

*In Vitro:* Relative to JAK2, Pacritinib (SB1518) is two-fold less potent against TYK2 (IC<sub>50</sub>=50 nM), 23-fold less potent against JAK3 (IC  $_{50}$ =520 nM) and 56-fold less potent against JAK1 (IC<sub>50</sub>=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<sub>50</sub> of 47 and 67 nM, respectively. Pacritinib inhibits Karpas 1106P and Ba/F3-JAK2<sup>V617F</sup> cells (which are cell lines dependent on JAK2 signaling) with IC<sub>50</sub> of 348 and 160 nM, respectively<sup>[1]</sup>. 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<sub>50</sub> of 80, 40, 33 and 29 nM, respectively. The IC<sub>50</sub> on auto-phosphorylation of FLT3-wt in RS4;11 is four-fold higher (IC<sub>50</sub>=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<sub>50</sub>=8 nM)<sup>[2]</sup>.

*In Vivo:* For evaluation of efficacy in the Ba/F3-JAK2<sup>V617F</sup> 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<sup>[1]</sup>. In rats, Pacritinib (SB1518) shows moderately fast absorption (t<sub>max</sub>=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<sub>max</sub>=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<sup>[3]</sup>.





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