# Product Introduction

## Pacritinib (SB1518)

Pacritinib (SB1518) is a potent and selective inhibitor of **Janus Kinase 2 (JAK2)** and **Fms-Like Tyrosine Kinase-3 (FLT3)** with **IC50s** of 23 and 22 nM, respectively.

### Technical Data:

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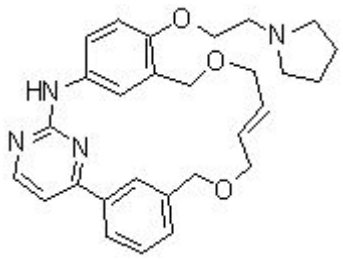
|---|---|---|
| **Molecular Weight (MW):** | 472.58 |  |
| **Formula:** | C28H32N4O3 | |
| **Solubility (25°C)** *** <1 mg/ml means slightly soluble or insoluble:** | DMSO 11 mg/mL heating (23 mM | |
| | Water <1 mg/mL (<1 mM) | |
| | Ethanol <1 mg/mL (<1 mM) | |
| **Purity:** | >98% | |
| **Storage:** | 3 years -20℃Powder | |
| | 6 months-80℃in DMSO | |
| **CAS No.:** | 937272-79-2 | |

### Biological Activity

Pacritinib is a potent inhibitor of both wild-type JAK2 and JAK2V617F mutant (IC50= 19 nM) that is present in high frequencies among patients with MPD. Relative to JAK2, Pacritinib is two-fold less potent against TYK2 (IC50= 50 nM), 23-fold less potent against JAK3 (IC50= 520 nM) and 56-fold less potent against JAK1 (IC50= 1280 nM). Pacritinib effectively permeates cells to modulate signaling pathways

downstream of JAK2, whether agonist activated or mutationally activated. Pacritinib induces apoptosis, cell cycle arrest and antiproliferative effects in JAK2WT- and JAK2V617F-dependent cells. Pacritinib inhibits cell proliferation of Karpas 1106P and Ba/F3-JAK2V617F with IC50 of 348 and 160 nM, respectively. Pacritinib inhibits endogenous colony growth derived from erythroid and myeloid progenitors with IC50 of 63 and 53 nM , respectively. [1] SB1518 also inhibits FLT3 and its mutant FLT3-D835Y(IC50= 6 nM ). Pacritinib inhibits FLT3 phosphorylation and downstream STAT, MAPK and PI3K signaling in FLT3-internal-tandem duplication (ITD), FLT3-wt cells and primary AML blast cells. Pacritinib treatment leads to a dose-dependent decrease of pFLT3, pSTAT5, pERK1/2 and pAkt in FLT3-ITD harboring MV4-11 cells with IC50 of 80, 40, 33 and 29 nM , respectively. Treatment of the primary AML blast cells with Pacritinib for 3 h leads to a dose-dependent decrease of pFLT3, pSTAT3 and pSTAT5 with an IC50 below 0.5 μM. Pacritinib induces apoptosis, cell cycle arrest and anti-proliferative effects in FLT3-mutant and FLT3-wt cells. Pacritinib inhibits cell proliferation of FLT3-ITD-harboring cells MV4-11 and primary AML blast cells with IC50s of 47 nM and 0.19-1.3 μM, respectively. [2]

Pacritinib administrated at 150 mg/kg p.o. q.d. to JAK2V617F-dependent xenograft model, significantly ameliorates splenomegaly and hepatomegaly symptoms, with 60% normalization of spleen weight and 92% normalization of liver weight and is well tolerated without significant weight loss or any hematological toxicities, including thrombocytopenia and anemia. Pacritinib induces dose-dependent inhibition of tumor growth of JAK2V617F-dependent SET-2 xenograft model (40% for 75 mg/kg and 61% for 150 mg/kg). [1] Pacritinib is efficacious in FLT3-ITD-bearing MV4-11 xenograft models. Pacritinib treated once daily for 21 consecutive days, induces dose-dependent inhibition of tumor growth (38% for 25 mg/kg, 92% for 50 mg/kg and 121% for 100 mg/kg). Complete regression is observed in 3/10 and 8/8 mice for the 50 and 100 mg/kg/day groups, respectively. [2]

Dual JAK2/FLT3 inhibitor that has progressed to Phase III clinical trials for treatment of Myelofibrosis

## References

1] Hart S, et al. Leukemia, 2011, 25(11), 1751-1759.
[2] Hart S, et al. Blood Cancer J, 2011, 1(11), e44.

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