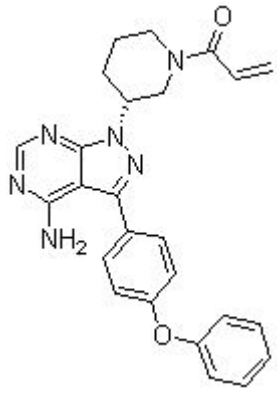
# Product Introduction

## Ibrutinib (PCI-32765)

Ibrutinib is a potent and highly selective **Btk** inhibitor with **IC50** of 0.5 nM, modestly potent to Bmx, CSK, FGR, BRK, HCK, less potent to EGFR, Yes, ErbB2, JAK3, etc.

### Technical Data:

| | | |
|---|---|---|
| **Molecular Weight (MW):** | 440.5 |  |
| **Formula:** | $C_{25}H_{24}N_6O_2$ | |
| **Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:** | DMSO 88 mg/mL | |
| | Water <1 mg/mL | |
| | Ethanol <1 mg/mL | |
| **Purity:** | >98% | |
| **Storage:** | 3 years -20℃Powder | |
| | 6 months-80℃in DMSO | |
| **CAS No.:** | 936563-96-1 | |

### Biological Activity

Ibrutinib shows the potent and irreversible inhibitory effect and selectivity for Btk enzymatic activity. In BCR pathway-activated DOHH2 cell line, Ibrutinib inhibits autophosphorylation of Btk, phosphorylation of Btk's physiological substrate PLCγ, and phosphorylation of further downstream kinase, ERK with IC50 of 11 nM, 29 nM and 13 nM, respectively. [1] Ibrutinib exhibits a significant dose-dependent and time-dependent induction of cytotoxicity in chronic lymphocytic leukemia (CLL) cells. In addition, Ibrutinib induces cell death depending on caspase pathway activation and antagonizes the ability of CLL cells to

proliferate after TLR signaling. [2] A recent study shows that Ibrutinib inhibits BCR-activated primary B cell proliferation with IC50 of 8 nM and results in inhibition of TNFα, IL-1β and IL-6 production in primary monocytes with IC50 of 2.6 nM, 0.5 nM and 3.9 nM, respectively. [3]

In a collagen-induced arthritis model, Ibrutinib significantly reduces clinical arthritis scores reflecting paw swelling and joint inflammation by inhibiting B-cell activation. In a MRL-Fas(lpr) lupus model, Ibrutinib reduces renal disease and autoantibody production. [1] In an adoptive transfer TCL1 mouse model of CLL, Ibrutinib (25 mg/kg/day) causes a transient early lymphocytosis, and delays CLL disease progression. [4]

## References


[1] Honigberg LA, et al. Proc Natl Acad Sci U S A. 2010, 107(29), 13075-13080.

[2] Herman SE, et al. Blood. 2011, 117(23), 6287-6296.

[3] Chang BY, et al. Arthritis Res Ther. 2011, 13(4), R115.

[4] Ponader S, et al. Blood. 2012, 119(5), 1182-1189.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