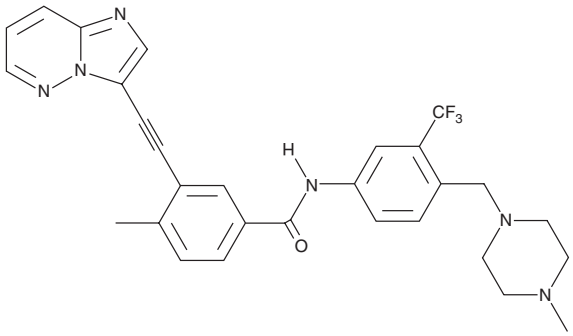
# PRODUCT INFORMATION

## Ponatinib

*Item No. 11494*



**CAS Registry No.:** 943319-70-8
**Formal Name:** 3-(2-imidazo[1,2-b]pyridazin-3-ylethynyl)-4-methyl-N-[4-[(4-methyl-1-piperazinyl)methyl]-3-(trifluoromethyl)phenyl]-benzamide
**Synonym:** AP 24534
**MF:** $C_{29}H_{27}F_3N_6O$
**FW:** 532.6
**Purity:** ≥98%
**UV/Vis.:** $\lambda_{max}$: 266, 301, 321 nm
**Supplied as:** A crystalline solid
**Storage:** -20°C
**Stability:** ≥4 years

*Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.*

### Laboratory Procedures

Ponatinib is supplied as a crystalline solid. A stock solution may be made by dissolving the ponatinib in the solvent of choice, which should be purged with an inert gas. Ponatinib is soluble in organic solvents such as DMSO and dimethyl formamide (DMF). The solubility of ponatinib in these solvents is approximately 20 mg/ml.

Ponatinib is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, ponatinib should first be dissolved in DMF and then diluted with the aqueous buffer of choice. Ponatinib has a solubility of approximately 0.25 mg/ml in a 1:3 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

### Description

Ponatinib is an orally bioavailable Bcr-Abl tyrosine kinase inhibitor ($IC_{50}$ = 0.37 nM).[1] It inhibits the tyrosine kinase inhibitor-resistant mutant Bcr-Abl$^{T315I}$ ($IC_{50}$ = 2 nM), as well as Bcr-Abl$^{Q252H}$, Bcr-Abl$^{Y253F}$, Bcr-Abl$^{M351T}$, and Bcr-Abl$^{H396P}$ mutants ($IC_{50}$s = 0.44, 0.3, 0.3, and 0.34 nM, respectively). It is selective for Bcr-Abl and these mutants over the insulin receptor, IGF-1R, Aurora A kinase, and Cdk2/cyclin E but does inhibit the receptor tyrosine kinases c-Src, VEGF receptor 2 (VEGFR2), FGFR1, and PDGFRα ($IC_{50}$s = 5.4, 1.5, 2.2, and 1.1 nM, respectively). Ponatinib inhibits proliferation of Ba/F3 cells expressing native ($IC_{50}$ = 0.5 nM) or mutant Bcr-Abl ($IC_{50}$s = 0.5-36 nM) and induces apoptosis. It reduces tumor growth in a Ba/F3 Bcr-Abl$^{T315I}$ mouse xenograft model when administered at doses ranging from 10 to 30 mg/kg. Formulations containing ponatinib have been used in the treatment of chronic-, accelerated-, or blast-phase chronic myeloid leukemia (CML), T315I-positive CML, or T315I-positive Philadelphia-chromosome positive acute lymphoblastic leukemia (Ph+ ALL).

### References


1. O'Hare, T., Shakespeare, W.C., Zhu, X., *et al.* AP24534, a pan-BCR-ABL inhibitor for chronic myeloid leukemia, potently inhibits the T315I mutant and overcomes mutation-based resistance. *Cancer Cell* **16(5),** 401-412 (2009).





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