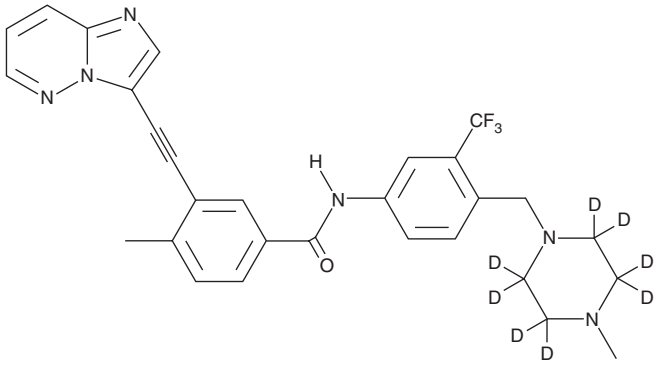
# PRODUCT INFORMATION

## Ponatinib-$d_8$

*Item No. 28905*



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| **CAS Registry No.:** | 1562993-37-6 |
| **Formal Name:** | 3-(2-imidazo[1,2-b]pyridazin-3-ylethynyl)-4-methyl-N-[4-[(4-methyl-1-piperazinyl-2,2,3,3,5,5,6,6-$d_8$)methyl]-3-(trifluoromethyl)phenyl]-benzamide |
| **MF:** | $C_{29}H_{19}D_8F_3N_6O$ |
| **FW:** | 540.6 |
| **Chemical Purity:** | ≥98% (Ponatinib) |
| **Deuterium Incorporation:** | ≥99% deuterated forms ($d_1$-$d_8$); ≤1% $d_0$ |
| **Supplied as:** | A 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-$d_8$ is intended for use as an internal standard for the quantification of ponatinib (Item No. 11494) by GC- or LC-MS. The accuracy of the sample weight in this vial is between 5% over and 2% under the amount shown on the vial. If better precision is required, the deuterated standard should be quantitated against a more precisely weighed unlabeled standard by constructing a standard curve of peak intensity ratios (deuterated *versus* unlabeled).

Ponatinib-$d_8$ is supplied as a solid. A stock solution may be made by dissolving the ponatinib-$d_8$ in the solvent of choice, which should be purged with an inert gas. Ponatinib-$d_8$ is soluble in methanol and DMSO.

### 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).

### Reference


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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