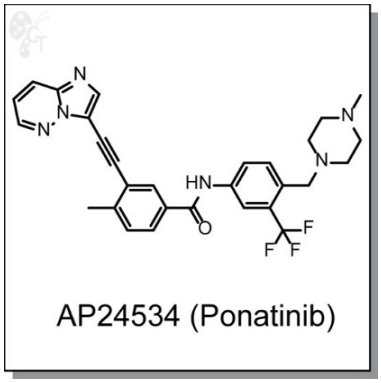
Product Specification Sheet

Product Name: AP24534 (Ponatinib)

Catalog Number: C2724



Technical information:

Chemical Formula:	$C_{29}H_{27}F_3N_6O$
CAS #:	943319-70-8
Molecular Weight:	532.57
Purity:	> 98%
Appearance:	White solid
Solubility:	Soluble in DMSO up to 100 mM
Chemical Name:	3-(2-(imidazo[1,2-b]pyridazin-3-yl)ethynyl)-4-methyl-N-(4-((4-methylpiperazin-1-yl)methyl)-3-(trifluoromethyl)phenyl)benzamide
Storage:	Store solid powder at 4°C desiccated; Store DMSO solution at -20°C.
Shelf Life:	In the unopened package, powder is stable for 1 year and DMSO solution is stable for 6 months under proper storage condition.

Handling:

- To make 10 mM stock solution, add 0.188mL of DMSO for each mg of AP24534 (Ponatinib)
- For DMSO solution, briefly spin the vial at 500 rpm in a 50 mL conical tube to ensure maximum sample recovery.

Biological Activity:

Ponatinib (AP24534) is a imidazopyridine-based pan-inhibitor of the kinases Abl, Abl(T315I), and other clinically important Abl kinase domain mutants at potencies of 0.37 nM, 2.0 nM, and 0.30-0.44 nM, respectively. Ponatinib also potently inhibits Src, VEGFR, FGFR, and PDGFR at 5.4, 1.5, 22, and 1.1 nM, respectively, while being >1000-fold selective over IGF-1R, Aurora A, andCDK2/Cyclin E. [1] In contrast to first- (imatinib) and second-line therapies (nilotinib, dasatinib) for CML, Ponatinib shows inhibition against the T31I mutant of Bcr-Abl.

In a panel of leukemic cell lines containing activating mutations in Flt3, Kit, or activating fusions of FGFR, PDGFRa, EOL1, and KG-1, Ponatinib inhibited phosphorylation of all four receptor tyrosine kinases in a dose dependent manner with IC50 values between 0.3 and 20 nM. [2] Apoptotic induction is believed to be the mechanism by which Ponatinib inhibits FLT3-ITD to in turn inhibit MV4-11 cell viability. [2]

Reference:

1. O'Hare et al., AP24534, a pan-BCR-ABL inhibitor for chronic myeloid leukemia, potently inhibits the T315I mutant and overcomes mutation-based resistance. Cancer Res. 2009, 16(5), 401-412. Pubmed ID: 19878872

2. Gozgit et al., Potent activity of ponatinib (AP24534) in models of FLT3-driven acute myeloid leukemia and other hematologic malignancies. Mol. Cancer. Ther. 2011, 10, 1028-1035. Pubmed ID: 21482694

To reorder: http://www.cellagentech.com/AP24534-Ponatinib/

For Technical Support: technical@cellagentech.com

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