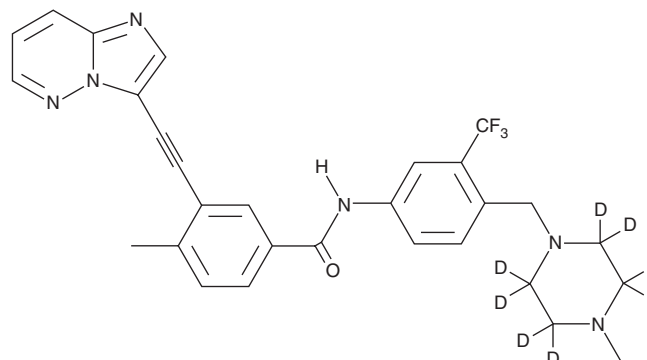


PRODUCT INFORMATION



Ponatinib-d₈ Item No. 28905

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-d₈]-methyl]-3-(trifluoromethyl)phenyl]-benzamide
MF: C₂₉H₁₉D₈F₃N₆O
FW: 540.6
Chemical Purity: ≥98% (Ponatinib)
Deuterium Incorporation: ≥99% deuterated forms (d₁-d₈); ≤1% d₀
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-d₈ 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-d₈ is supplied as a solid. A stock solution may be made by dissolving the ponatinib-d₈ in the solvent of choice, which should be purged with an inert gas. Ponatinib-d₈ is soluble in methanol and DMSO.

Description

Ponatinib is an orally bioavailable Bcr-Abl tyrosine kinase inhibitor (IC₅₀ = 0.37 nM).¹ It inhibits the tyrosine kinase inhibitor-resistant mutant Bcr-Abl^{T315I} (IC₅₀ = 2 nM), as well as Bcr-Abl^{Q252H}, Bcr-Abl^{Y253F}, Bcr-Abl^{M351T}, and Bcr-Abl^{H396P} mutants (IC₅₀s = 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 (IC₅₀s = 5.4, 1.5, 2.2, and 1.1 nM, respectively). Ponatinib inhibits proliferation of Ba/F3 cells expressing native (IC₅₀ = 0.5 nM) or mutant Bcr-Abl (IC₅₀s = 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).

WARNING

THIS PRODUCT IS FOR RESEARCH ONLY - NOT FOR HUMAN OR VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

SAFETY DATA

This material should be considered hazardous until further information becomes available. Do not ingest, inhale, get in eyes, on skin, or on clothing. Wash thoroughly after handling. Before use, the user must review the complete Safety Data Sheet, which has been sent via email to your institution.

WARRANTY AND LIMITATION OF REMEDY

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