

Product Data Sheet

Product Name: PD 166326

Cat. No.: GC15314

Chemical Properties

Cas. No. 185039-91-2

Chemical Name 6-(2,6-dichlorophenyl)-2-[[3-(hydroxymethyl)phenyl]amino]-8-methyl-pyrido[2,3-d]pyrimidin-7(8H)-one

SMILES OCC1=CC=CC(NC2=NC(N(C)C(C(C3=C(Cl)C=CC=C3Cl)=C4)=O)=C4C=N2)=C1

Formula $C_{21}H_{16}Cl_2N_4O_2$

M.Wt 427.3

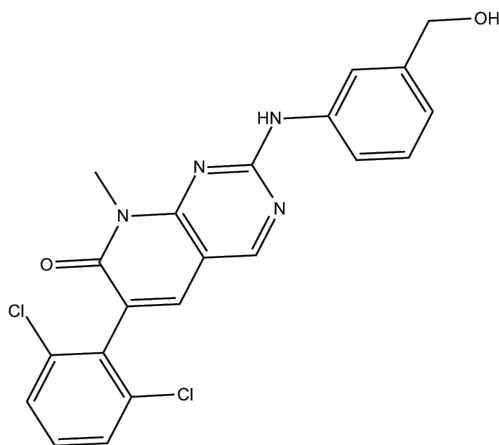
Solubility $\leq 25\text{mg/ml}$ in DMSO; 25mg/ml in dimethyl formamide

Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



Background

IC₅₀: 8 nM for c-abl

PD 166326 is a receptor tyrosine kinase inhibitor.

Receptor tyrosine kinases are the high-affinity cell surface receptors for many growth factors,

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Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

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cytokines, as well as hormones. They have been shown not only to be critical regulators of normal cellular processes but also to have a key role in the development of many types of cancer.

In vitro: PD 166326 was identified as a pyridopyrimidine-type inhibitor of receptor tyrosine kinases inhibiting c-abl and Bcr/Abl-dependent cell growth. In addition, PD 166326 could also potently inhibit c-src. Moreover, PD166326 was found to be superior to imatinib mesylate in inhibiting the constitutive tyrosine phosphorylation of numerous leukemia-cell proteins, such as the src family member Lyn [1, 2].

In vivo: In mice with the CML-like disease, PD166326 could rapidly inhibit Bcr/Abl kinase activity after a single po dose and showed great antileukemic activity. It was found that 70% of PD166326-treated mice achieved a white blood cell count less than $20.0 \times 10^9/L$ at necropsy, compared with 8% of imatinib mesylate-treated animals. Furthermore, 2/3 of PD166326-treated mice had complete resolution of splenomegaly, compared with none of the imatinib mesylate-treated animals. In addition, PD166326 could also prolong the survival of mice with imatinib mesylate-resistant CML induced by the Bcr/Abl mutants of P210/H396P and P210/M351T [2].

Clinical trial: So far, no clinical study has been conducted.

References:

- [1] Wisniewski, D. ,Lambek, C.L.,Liu, C., et al. Characterization of potent inhibitors of the Bcr-Abl and the c-kit receptor tyrosine kinases. *Cancer Research* 62(15), 4244-4255 (2002).
- [2] Wolff, N. C.,Veach, D.R.,Tong, W.P., et al. PD166326, a novel tyrosine kinase inhibitor, has greater antileukemic activity than imatinib mesylate in a murine model of chronic myeloid leukemia. *Blood* 105(10), 3995-4003 (2005).

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