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	≤25mg/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 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	PD 166326		

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, 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

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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 × 109/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).