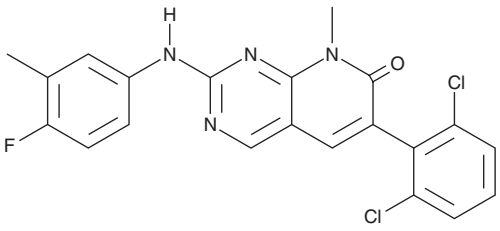
PRODUCT INFORMATION

PD 180970

Item No. 30619

CAS Registry No.: 287204-45-9
Formal Name: 6-(2,6-dichlorophenyl)-2-[(4-fluoro-3-methylphenyl)amino]-8-methyl-pyrido[2,3-d]pyrimidin-7(8H)-one
MF: $C_{21}H_{15}Cl_2FN_4O$
FW: 429.3
Purity: ≥98%
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

PD 180970 is supplied as a solid. A stock solution may be made by dissolving the PD 180970 in the solvent of choice, which should be purged with an inert gas. PD 180970 is soluble in the organic solvent DMSO at a concentration of approximately 20 mg/ml.

Description

PD 180970 is an inhibitor of Bcr-Abl.[1] It inhibits wild-type and mutant forms of Bcr-Abl, as well as the p210 isoform, a marker of chronic myelogenous leukemia (CML), with IC_{50} values ranging from 5 to 48 nM.[1,2] PD 180970 is selective for Bcr-Abl over basic FGFR (bFGFR) and PDGFR (IC_{50}s = 934 and 1,430 nM, respectively) but also inhibits Src, LCK, KIT, and EGFR (IC_{50}s = 0.8, <5, 50, and 390 nM, respectively).[3,4] It induces cell cycle arrest at the G_1 phase and apoptosis in K562 CML cells when used at a concentration of 50 nM.[5] PD 180970 (500 nM) inhibits constitutive STAT3 DNA-binding activity in, and proliferation of, MDA-MB-468 breast cancer cells.[6] It also inhibits proliferation of Ba/F3 cells expressing mutant p210 Bcr-Abl^{Y253F} that are resistant to imatinib (Item No. 13139) with an IC_{50} value of 48 nM.[2]

References

1. Dorsey, J.F., Jove, R., Kraker, A.J., *et al.* The pyrido[2,3-d]pyrimidine derivative PD180970 inhibits p210$^{Bcr-Abl}$ tyrosine kinase and induces apoptosis of K562 leukemic cells. *Cancer Res.* **60(12)**, 3127-3131 (2000).
2. La Rosée, P., Corbin, A.S., Stoffregen, E.P., *et al.* Activity of the Bcr-Abl kinase inhibitor PD180970 against clinically relevant Bcr-Abl isoforms that cause resistance to imatinib mesylate (Gleevec, STI571). *Cancer Res.* **62(24)**, 7149-7153 (2002).
3. Kraker, A.J., Hartl, B.G., Amar, A.M., *et al.* Biochemical and cellular effects of c-Src kinase-selective pyrido[2, 3-d]pyrimidine tyrosine kinase inhibitors. *Biochem. Pharmacol.* **60(7)**, 885-898 (2000).
4. Corbin, A.S., Griswold, I.J., La Rosée, P., *et al.* Sensitivity of oncogenic KIT mutants to the kinase inhibitors MLN518 and PD180970. *Blood* **104(12)**, 3754-3757 (2004).
5. Huang, M., Dorsey, J.F., Epling-Burnette, P.K., *et al.* Inhibition of Bcr–Abl kinase activity by PD180970 blocks constitutive activation of Stat5 and growth of CML cells. *Oncogene* **21(57)**, 8804-8816 (2002).
6. Garcia, R., Bowman, T.L., Niu, G., *et al.* Constitutive activation of Stat3 by the Src and JAK tyrosine kinases participates in growth regulation of human breast carcinoma cells. *Oncogene* **20(20)**, 2499-2513 (2001).

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