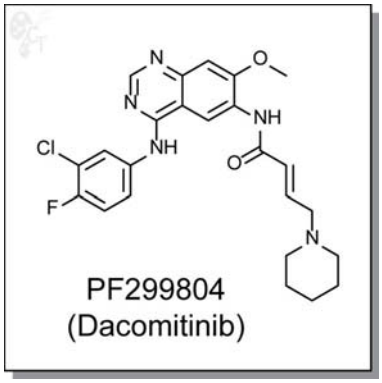
Cellagen Technology

Product Specification Sheet

Product Name: PF-299804 (Dacomitinib)

Catalog Number: C7299



Technical information:

Chemical Formula:	$C_{24}H_{25}ClFN_5O_2$
CAS #:	1110813-31-4
Molecular Weight:	469.94
Purity:	> 99%
Appearance:	White solid
Solubility:	Soluble in DMSO up to 50 mM
Chemical Name:	(E)-N-(4-(3-chloro-4-fluorophenylamino)-7-methoxyquinazolin-6-yl)-4-(piperidin-1-yl)but-2-enamide
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 0.213mL of DMSO for each mg of PF-299804 (Dacomitinib).
- For DMSO solution, briefly spin the vial at 500 rpm in a 50 mL conical tube to ensure maximum sample recovery.

Biological Activity:

PF299804 (Dacomitinib) is an orally-available, aminoquinazoline-based, irreversible pan-HER inhibitor with IC50s of 6, 46, and 74 nM for ErbB1, ErbB2, and ErbB4, respectively. PF299804 inhibits ErbB1 autophosphorylation in A431 cells with an IC50 of 15 nM. [1]

PF299804 is known to be efficacious against EGFR-activating mutations as well as the common EGFR T790M resistance mutation which is less responsive to other therapies such as gefitinib and erlotinib. Cellular activity against EGFR and ErbB2 (NIH3T3) are 6 and 41 nM, respectively. [2]

PF299804 induces apoptosis and G1 arrest and inhibits downstream signaling pathways such as STAT3, AKT, and ERK in HER2-amplified gastric cancer cells. It is synergistic with trastuzumab as well as a host of other kinase inhibitors (IGF1R, ERK1/2, PI3K/mTOR). [3]

In a panel of almost 50 breast cancer cell lines, PF299804 induced G0 and G1 cell-cycle arrest with IC50s ranging from 5 nM to 5 uM and was active against cell lines that had acquired resistance to therapies such as trastuzumab and lapatinib. [4]

Reference:

1. Gonzales et al., Antitumor activity and pharmacokinetic properties of PF-00299804, a second-generation irreversible pan-erbB receptor tyrosine kinase inhibitor. Mol. Cancer. Ther. 2008, 7, 1880-1889. Pubmed ID: 18606718
2. Engelman et al., PF00299804, an irreversible pan-ERBB inhibitor, is effective in lung cancer models with EGFR and ERBB2 mutations that are resistant to gefitinib. Cancer Res. 2007, 67(24), 11924-11932. Pubmed ID: 18089823
3. Nam et al., Evaluation of the antitumor effects and mechanisms of PF00299804, a pan-HER inhibitor, alone or in combination with chemotherapy or targeted agents in gastric cancer. Mol. Cancer. Ther. 2012, 11, 439-451. Pubmed ID: 22135232
4. Kalous et al., Dacomitinib (PF-00299804), an irreversible Pan-HER inhibitor, inhibits proliferation of HER2-amplified breast cancer cell lines resistant to trastuzumab and lapatinib. Mol. Cancer Ther. 2012, 11, 1978-1987. Pubmed ID: 22761403

To reorder: http://www.cellagentech.com/PF-299804-Dacomitinib/

For Technical Support: technical@cellagentech.com

Chemicals are sold for research use only, not for clinical or diagnostic use.