ALPHA DIAGNOSTIC INTERNATIONAL

Product Specification Sheet

Life Technologies™ Your Molecular & Cell Technology Partner

□ **Cat. #** SM-101070-10	Canertinib (CI-1033), kinase Inhibitor of Her2/Erb2/EGFR (mol wt 485; >98%)	**SIZE:** 10 mg
□ **Cat. #** SM-101070-50	Canertinib (CI-1033), kinase Inhibitor of Her2/Erb2/EGFR (mol wt 485; >98%)	**SIZE:** 50 mg

Canertinib (CI-1033) is an experimental drug candidate for the treatment of cancer. It is a potent and selective inhibitor of tyrosine residue phosphorylation of EGFR, blocking signal transgression and ceasing angiogenisis. It is an irreversible tyrosine-kinase inhibitor with activity against EGFR (IC50 0.8 nM), HER-2 (IC50 19 nM) and ErbB-4 (IC50 7 nM).

Canertinib binds to the intracellular domains of epidermal growth factor receptor tyrosine kinases (ErbB family), irreversibly inhibiting their signal transduction functions and resulting in tumor cell apoptosis and suppression of tumor cell proliferation. It not only inhibits tyrosine phosphorylation but also enhances ubiquitinylation and accelerates endocytosis and subsequent intracellular destruction of ErbB-2 molecules. Canertinib alkylates a cysteine residue specific to ErbB receptors. The degradative pathway of ErbB receptor tyrosine kinases stimulated by tyrosine kinase inhibitors appears to be chaperone mediated, and thus is similar to the pathways activated by the heat shock protein 90 (Hsp90) antagonist geldanamycin and by stress-induced mechanisms.

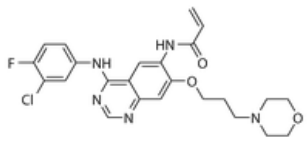
Additionally, Canertinib's action in inhibiting EGFR increases apoptosis in cancerous cell lines.

Biological activity:

In vitro: CI-1033 shows excellent potency for irreversible inhibition of erbB2 auto phosphorylation in MDA-MB 453 cells. CI-1033 also shows high permeability in Caco-2 cells and inhibits secretory transport of vinblastine, which indicates that CI-1033 is a likely inhibitor of the P-gp CI-1033 alone, significantly suppresses constitutively activated Akt and MAP kinase. In combination with gemcitabine, CI-1033 inhibits Akt and prevents increased levels of MAPK phosphorylation. CI-1033 stimulates p27 expression and p38 phosphorylation in MDA-MB-453 cells. CI-1033 is highly specific to the erbB receptor family and not sensitive to PGFR, FGFR or IR even at 50 µM. CI-1033 shows high levels of inhibition in A431 cells expressing EGFR with IC50 of 7.4 nM. CI-1033 suppresses heregulin-stimulated tyrosine phosphorylation of erbB2, erbB3 and erbB4 with IC50 of 5, 14 and 10 nM, respectively. CI-1033 also inhibits expression of pp62c-fos in response to heregulin

In vivo: CI-1033 shows impressive activity against A431 xenografts in nude mice at 5 mg/kg of body weight. CI-1033 (20 to 80 mg/kg/d) achieves a high degree of tumor regressions in H125 xenograft models. Oral administration of CI-1033 causes a marked inhibition of growth in TT, TE6 and TE10 xenografts in nude mice, without animal death and <10% weight loss

Properties



Mol Wt: 485.94
Form: Powder
Purity >95%

Formula C24H25ClFN5O3
CAS No. 267243-28-7
Synonyms PD183805
Solubility in vitro: Water, <1 mg/mL, Ethanol 9 mg/m
In Vivo: 30% propylene glycol, 5% tween 80, 65%D5W
Chemical Name N-(4-(3-chloro-4-fluorophenylamino)-7-(3-morpholinopropoxy) quinazolin-6-yl)acrylamide

Do not freeze and thaw.

Storage:

Store powder at -20oC for up to 3 years.
Upto 6 months-80°Cin DMSO

Stability: 6-12 months at –20°C or below.

Shipping: 4°C for solutions and room temp for powder

General References: Vivanco I, et al (2012) Cancer Discov 2(5):458-71; Choi W, et al. (2010) J Cell Sci 123(Pt 18):3102-11; Dong Z, et al. (2010) Carcinogenesis ;31(11):1948-55

*This product is for research use only.

Related items:

SM-101000-5 EGFR/HER2 kinase inhibitor (>99%, M.wt 485.94) (Afatinib/BIBW-2992
SM-101000-50 EGFR/HER2 kinase inhibitor (>99%, M.wt 485.94) (Afatinib/BIBW-2992
SM-101010-5 Inhibitor of EGFR/HER family (Her1, Her2, Her3 or Pan Her-inhibitor) (BMS-59926/AC480, Mol wt 567.01, >99%)
SM-101010-50 Inhibitor of EGFR/HER family (Her1, Her2, Her3 or Pan Her-inhibitor) (BMS-59926/AC480, Mol wt 567.01, >99%)
SM-101020-10 Inhibitor of EGFR/HDAC/Her2 (CUDC-101; 7-((4-((3-ethynylphenyl)amino)-7-methoxyquinazolin-6-yl)oxy)-N-hydroxyheptanamide, Mol wt 434.49, >99%)
SM-101020-50 Inhibitor of EGFR/HDAC/Her2 (CUDC-101; 7-((4-((3-ethynylphenyl)amino)-7-methoxyquinazolin-6-yl)oxy)-N-hydroxyheptanamide, Mol wt 434.49, >99%)
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SM-101000-50 141210P

Alpha Diagnostic Intl Inc., 6203 Woodlake Center Dr, San Antonio, TX 78244, USA; **Email**: service@4adi.com

India Contact:
Life Technologies (India) Pvt. Ltd.
306, Aggarwal City Mall, Opposite M2K Pitampura, Delhi – 110034 (INDIA). Ph: +91-11-42208000, 42208111, 42208222, Mobile: +91-9810521400, Fax: +91-11-42208444
Email: customerservice@lifetechindia.com Website: www.lifetechindia.com