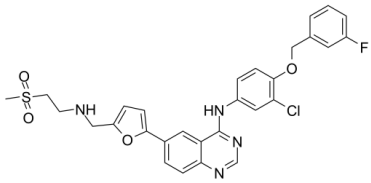
Data Sheet

Product Name:	Lapatinib
Cat. No.:	CS-0036
CAS No.:	231277-92-2
Molecular Formula:	C29H26ClFN4O4S
Molecular Weight:	581.06
Target:	Autophagy; EGFR; Ferroptosis
Pathway:	Apoptosis; Autophagy; JAK/STAT Signaling; Protein Tyrosine Kinase/RTK
Solubility:	DMSO : ≥ 39 mg/mL (67.12 mM)



BIOLOGICAL ACTIVITY:

Lapatinib (GW572016) is a potent inhibitor of the **ErbB-2** and **EGFR** tyrosine kinase domains with **IC_{50}** values against purified **EGFR** and **ErbB-2** of 10.2 and 9.8 nM, respectively[1]. IC50 & Target: IC50: 10.2 nM (EGFR), 9.8 nM (ErbB2)[1] **In Vitro:** Lapatinib (GW2016; 0.03-10 μM; 6 hours; BT474 and HN5 cells) treatment inhibits receptor autophosphorylation of EGFR and ErbB-2 in a dose-responsive manner. Phosphorylation of serine 473 of AKT was inhibited by GW2016 in a dose-dependent manner[1].

Lapatinib (GW2016; 72 hours; HN5, A-43, BT474, N87, and CaLu-3 cells) treatment has a selective inhibition of the proliferation of human tumor cell lines[1].

Lapatinib (GW2016; 1-10 μM; 72 hours; HN5 cells) treatment results in induces G1 arrest[1]. **In Vivo:** Lapatinib (GW2016; 30-100 mg/kg; oral administration; twice daily; for 21 days; CD-1 nude female mice) treatment inhibits tumor xenograft growth of the HN5 cells in a dose-responsive manner at 30 and 100 mg/kg, with complete inhibition of tumor growth at the higher dose[1].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [1]The intracellular kinase domains of EGFR, ErbB-2, and ErbB4 are purified from a baculovirus expression system. EGFR, ErbB-2, and ErbB-4 reactions are performed in 96-well polystyrene round-bottomed plates in a final volume of 45 μL. Reaction mixtures contain 50 mM 4-morpholinepropanesulfonic acid (pH 7.5), 2 mM $MnCl_2$, 10 μM ATP, 1 μCi of [γ-^{33}P] ATP/reaction, 50 μM Peptide A [Biotin-(amino hexonoic acid)-EEEEYFELVAKKK-CONH2], 1 mM dithiothreitol, and 1 μL of DMSO containing serial dilutions of Lapatinib beginning at 10 μM. The reaction is initiated by adding the indicated purified type-1 receptor intracellular domain. The amount of enzyme added is 1 pmol/reaction (20 nM). Reactions are terminated after 10 min at 23°C by adding 45 μL of 0.5% phosphoric acid in water. The terminated reaction mix (75 μL) is transferred to phosphocellulose filter plates. The plates are filtered and washed three times with 200 μL of 0.5% phosphoric acid. Scintillation cocktail (50 μL) is added to each well, and the assay is quantified by counting in a Packard Topcount[1]. **Cell Assay:** Lapatinib (GW2016) is dissolved in DMSO and stored, and then diluted with appropriate media (DMSO 0.3%) before use[1].[1]Cells are plated in 96-well plates, in the media, at the following densities: HFF and HN5, 1000 cells/well and BT474, 5000 cells/well. After 24 h, the cells are exposed to vehicle (0.3% DMSO) or Lapatinib (1 nM, 10 nM, 100 nM, 1μM, 10μM, and 100μM). Lapatinib is removed from the cells after 72 h and is replaced by either DMEM containing 10% FBS and 50 μg/mL Gentamicin (HFF and HN5) or RPMI containing 10% FBS and 50 μg/mL Gentamicin (BT474). Methylene blue staining is performed at the time points over a total period of 16 days[1]. **Animal Administration:** Lapatinib (GW2016) is prepared in sulfo-butyl-ether-β-cyclodextrin 10% aqueous solution (Mice)[1].[1][3]Mice[1]

CD-1 nude female mice are used for HN5 human tumor xenografts, which are initiated by injection of a cell suspension in PBS:Matrigel (1:1). C.B-17 SCID female mice are used for BT474 human tumor xenografts, which are initiated by implantation of tumor fragments (20-100 mg) from established tumors. Tumor cells and fragments are implanted by s.c. injection in the right flank. The s.c. tumors are measured with calipers, and mice are weighed twice weekly. Tumor weight is estimated from tumor volume using this formula: length×width^2/2=tumor volume (mm^3). Treatment begins when tumors are palpable, 3-5 mm in diameter. Lapatinib (30 and

100 mg/kg) is administered p.o. twice daily for 21 days in a vehicle of sulfo-butyl-ether-β-cyclodextrin 10% aqueous solution (CD10).
Rats[3]
Wistar rats (12-week-old albino males) are randomly assigned to three groups: control (C, n=8), Trastuzumab (T, n=8) and Lapatinib (L, n=8) treatments. The control animals are untreated, but the others in groups T and Lapatinib are administered with the chemotherapy drugs. Trastuzumab is delivered once at a dose of 10 mg/kg/day via intraperitoneal injection on the first day of the study. Lapatinib is administered daily at a dose of 100 mg/kg/day by oral gavage for 7 consecutive days. The selected doses are equivalent to those used in the clinics. On day 8, anesthesia is induced by a single intraperitoneal injection of ketamine and xylazine (50 and 5 mg/kg, respectively). The blood samples are collected and the hearts are removed for biochemical analysis.

References:

[1]. Rusnak DW, et al. The effects of the novel, reversible epidermal growth factor receptor/ErbB-2 tyrosine kinase inhibitor, GW2016, on the growth of human normal and tumor-derived cell lines in vitro and in vivo. Mol Cancer Ther. 2001 Dec;1(2):85-94

CAIndexNames:

4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-

SMILES:

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