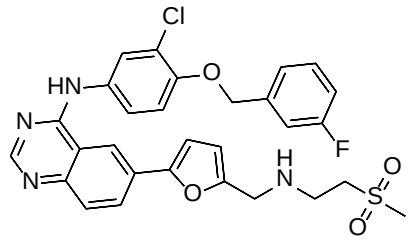
Product data sheet

MedKoo Cat#: 100490A Name: Lapatinib (free base) CAS#: 231277-92-2 (free base) Chemical Formula: $C_{29}H_{26}ClFN_4O_4S$ Exact Mass: 580.1347 Molecular Weight: 581.06	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
Lapatinib is a synthetic, orally-active quinazoline with potential antineoplastic activity. Lapatinib reversibly blocks phosphorylation of the epidermal growth factor receptor (EGFR), ErbB2, and the Erk-1 and-2 and AKT kinases; it also inhibits cyclin D protein levels in human tumor cell lines and xenografts. EGFR and ErbB2 have been implicated in the growth of various tumor types. Check for active clinical trials or closed clinical trials using this agent.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMF	20.0	34.42
DMSO	65.70	113.07
DMSO:PBS (pH 7.2) (1:2)	0.33	0.57

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	1.72 mL	8.60 mL	17.21 mL
5 mM	0.34 mL	1.72 mL	3.44 mL
10 mM	0.17 mL	0.86 mL	1.72 mL
50 mM	0.03 mL	0.17 mL	0.34 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Mu Y, Sun D. Lapatinib, a Dual Inhibitor of Epidermal Growth Factor Receptor (EGFR) and HER-2, Enhances Radiosensitivity in Mouse Bladder Tumor Line-2 (MBT-2) Cells In Vitro and In Vivo. Med Sci Monit. 2018 Aug 20;24:5811-5819. doi: 10.12659/MSM.909865. PMID: 30125265; PMCID: PMC6113922.
2. Sakai K, Maeda S, Saeki K, Nakagawa T, Murakami M, Endo Y, Yonezawa T, Kadosawa T, Mori T, Nishimura R, Matsuki N. Anti-tumour effect of lapatinib in canine transitional cell carcinoma cell lines. Vet Comp Oncol. 2018 Dec;16(4):642-649. doi: 10.1111/vco.12434. Epub 2018 Sep 23. PMID: 30246405.

In vivo study

1. Mu Y, Sun D. Lapatinib, a Dual Inhibitor of Epidermal Growth Factor Receptor (EGFR) and HER-2, Enhances Radiosensitivity in Mouse Bladder Tumor Line-2 (MBT-2) Cells In Vitro and In Vivo. Med Sci Monit. 2018 Aug 20;24:5811-5819. doi: 10.12659/MSM.909865. PMID: 30125265; PMCID: PMC6113922.

Product data sheet

2. Sakai K, Maeda S, Saeki K, Nakagawa T, Murakami M, Endo Y, Yonezawa T, Kadosawa T, Mori T, Nishimura R, Matsuki N. Anti-tumour effect of lapatinib in canine transitional cell carcinoma cell lines. Vet Comp Oncol. 2018 Dec;16(4):642-649. doi: 10.1111/vco.12434. Epub 2018 Sep 23. PMID: 30246405.

7. Bioactivity

Biological target: Lapatinib (GW572016) is an inhibitor of the ErbB-2 and EGFR tyrosine kinase domains with IC50 values against purified EGFR and ErbB-2 of 10.2 and 9.8 nM, respectively.

In vitro activity

Lapatinib, in combination with radiation, enhanced DNA damage in MBT-2 cells. The results of immunofluorescence staining showed the presence of γ-H2AX, which is a marker of damage to double-strand DNA (Figure 5A). The control group of cells showed the complete absence or least number of γ-H2AX foci (0±0.01/cell); the cells receiving only radiation showed signs of DNA damage with γ-H2AX foci of 14.2±0.35/cell at 30 min; treatment with lapatinib alone was ineffective in causing DNA damage and resulted in no alterations in γ-H2AX foci (0±0.25/cell). However, in MBT-2 cells pretreated with lapatinib and exposed to radiation, there was a significant increase in the number of γ-H2AX foci (22.1±0.50/cell) ($P<0.001$) compared with cells exposed to radiation alone (14.2±0.35/cell). The results of Western blot showed a dose-dependent change in the levels of γ-H2AX in cells pretreated with lapatinib (50 and 100 nM) followed by radiation of dose 2.5 and 10 Gy (Figure 5B).

Reference: Med Sci Monit. 2018 Aug 20;24:5811-5819. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6113922/

In vivo activity

The outcomes of lapatinib treatment of tumor xenografts in an animal model showed that a daily dose of lapatinib (oral, 200 mg/kg/day) for seven days, combined with radiation on the fourth day caused a significant suppression in the growth of xenografts tumors compared with irradiation alone (Figure 6A). The results suggested that an oral dose of lapatinib increased the radiation-mediated suppression of xenografts tumors by about 60%. The results of immunohistochemistry for expression of HER-2 and EGFR in tumors recovered from mice at the end of treatment protocol of seven days showed the involvement of radiation in enhancing the levels of EGFR and HER-2 (Figure 6B). However, lapatinib, in combination with radiation therapy, suppressed the radiation-mediated activation of EGFR and HER-2 in xenograft tumors. The outcomes of this in vivo experiment indicated that lapatinib induced radiosensitization by inhibiting the radiation-mediated expression of EGFR and HER-2, in addition to facilitating DNA damage.

Reference: Med Sci Monit. 2018 Aug 20;24:5811-5819. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6113922/