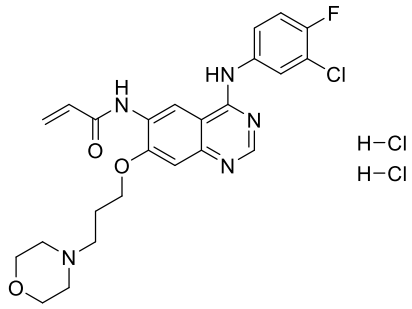
Product data sheet

MedKoo Cat#: 200600 Name: Canertinib HCl CAS#: 289499-45-2 (HCl) Chemical Formula: $C_{24}H_{27}Cl_3FN_5O_3$ Molecular Weight: 558.86	
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:

Canertinib, also known as CI1033 and PD183805, is a potent ErbB inhibitor for the treatment of cancer. 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). By 2015, Pfizer had discontinued development of the drug. Canertinib has been reported as a substrate for OATP1B3. Interaction of canertinib with OATP1B3 may alter its hepatic disposition and can lead to transporter mediated drug-drug interactions. Also, canertinib is not an inhibitor of OATP-1B1 or OATP-1B3 transporter.

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
DMSO	50	89.47

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	1.79 mL	8.95 mL	17.89 mL
5 mM	0.36 mL	1.79 mL	3.58 mL
10 mM	0.18 mL	0.89 mL	1.79 mL
50 mM	0.04 mL	0.18 mL	0.36 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. Djerf Severinsson EA, Trinks C, Gréen H, Abdiu A, Hallbeck AL, Stål O, Walz TM. The pan-ErbB receptor tyrosine kinase inhibitor canertinib promotes apoptosis of malignant melanoma in vitro and displays anti-tumor activity in vivo. Biochem Biophys Res Commun. 2011 Oct 28;414(3):563-8. doi: 10.1016/j.bbrc.2011.09.118. Epub 2011 Oct 1. PMID: 21982771.

2. Ako E, Yamashita Y, Ohira M, Yamazaki M, Hori T, Kubo N, Sawada T, Hirakawa K. The pan-erbB tyrosine kinase inhibitor CI-1033 inhibits human esophageal cancer cells in vitro and in vivo. Oncol Rep. 2007 Apr;17(4):887-93. doi: 10.3892/or.17.4.887. PMID: 17342332.

In vivo study

1. Djerf Severinsson EA, Trinks C, Gréen H, Abdiu A, Hallbeck AL, Stål O, Walz TM. The pan-ErbB receptor tyrosine kinase inhibitor canertinib promotes apoptosis of malignant melanoma in vitro and displays anti-tumor activity in vivo. Biochem Biophys Res Commun. 2011 Oct 28;414(3):563-8. doi: 10.1016/j.bbrc.2011.09.118. Epub 2011 Oct 1. PMID: 21982771.

2. Ako E, Yamashita Y, Ohira M, Yamazaki M, Hori T, Kubo N, Sawada T, Hirakawa K. The pan-erbB tyrosine kinase inhibitor CI-1033 inhibits human esophageal cancer cells in vitro and in vivo. Oncol Rep. 2007 Apr;17(4):887-93. doi: 10.3892/or.17.4.887. PMID: 17342332.

7. Bioactivity

Biological target:

Canertinib dihydrochloride (CI-1033 dihydrochloride) is a potent and irreversible EGFR inhibitor; inhibits cellular EGFR and ErbB2 autophosphorylation with IC50s of 7.4 and 9 nM.

In vitro activity

Canertinib treatment of RaH3 and RaH5 with increasing concentrations (0–10 μM) for 72 h decreased the number of living cells in a dose-dependent manner (Fig. 1). Half-maximum growth inhibitory concentration (IC50), i.e. the dose required to inhibit serum stimulated growth by 50%, was estimated to 0.78 ± 0.08 μM in RaH3 and 0.80 ± 0.02 μM in RaH5. 5 μM canertinib completely inhibited growth ($P < 0.01$) and concentrations >5 μM induced dose-dependent cell death in both cell lines. Canertinib treatment of RaH3 and RaH5 cells with 1 μM for 24 h accumulated cells in the G1-phase of the cell cycle with a concomitant decrease in the S and G2/M cell cycle phase (Fig. 1C–F, Supplementary Table S1). Treatment of RaH3 and RaH5 cells with 10 μM of canertinib for up to 20 h decreased the number of cells in all cell cycle phases, also a time-dependent apoptotic sub-fraction of G1 cells appeared (Supplementary Fig. S1). Canertinib-induced apoptosis was confirmed by the Annexin V method, a time-dependent increase in apoptotic RaH3 and RaH5 cells occurred within 72 h of drug-exposure with 10 μM (Fig. 2C and D). Maximum apoptosis was achieved in RaH3 cells within 72 h (79%, $P < 0.01$) and in RaH5 cells within 48 h (76%, $P < 0.001$) of treatment (Fig. 2C and D). RaH3 and RaH5 cells treated with concentrations $\geqslant$7.5 μM of canertinib for 48 h clearly induced apoptosis and with 10 μM apoptosis occurred in 56% ($P < 0.05$) and 76% ($P < 0.001$) of RaH3 and RaH5 cells, respectively (Fig. 2E and F). ErbB1 and ErbB3 phosphorylation was abolished within 30 min of 1 μM canertinib treatment of RaH3 and RaH5 and remained undetectable during the 6 h observation period as determined by Western blot (Fig. 3A). Canertinib treatment of RaH3 and RaH5 with 1 μM reduced Akt and Erk1/2 phosphorylation already within 30 min of incubation in both cell lines (Fig. 3B).

Reference: Biochem Biophys Res Commun. 2011 Oct 28;414(3):563-8. https://linkinghub.elsevier.com/retrieve/pii/S0006-291X(11)01733-5

In vivo activity

The growth of human malignant melanoma xenografts, RaH3 and RaH5, in nude mice was significantly inhibited by i.p. injections of 40 mg/kg/day canertinib (Fig. 4). The anti-proliferative effect on melanoma xenografts was visible already within 4 days of treatment and further increased throughout the treatment period as observed through the differences in tumor volumes, reaching statistical significance within 18 days of treatment (RaH3 $P = 0.021$ and RaH5 $P = 0.014$) (Fig. 4A and B). The growth inhibition of canertinib on RaH3 and RaH5 xenografts was also reflected by a significant decrease in tumor weights as compared to untreated tumors (Fig. 4C). The detectable side effects were mild including less than 8% weight loss in the treated mice compared to untreated animals, with no signs of skin rash, diarrhea or any other side effect, all animals seemed to thrive despite treatment. However, one RaH5 xenograft-bearing mouse died in the treatment group at day 5 without showing any signs of illness.

Reference: Biochem Biophys Res Commun. 2011 Oct 28;414(3):563-8. https://linkinghub.elsevier.com/retrieve/pii/S0006-291X(11)01733-5

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.