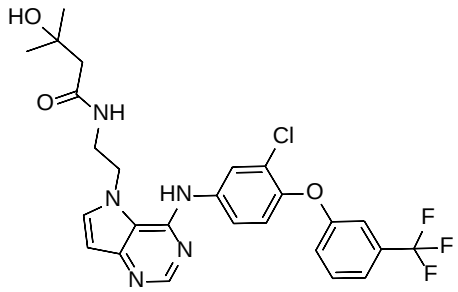
Product data sheet

MedKoo Cat#: 202721 Name: TAK-285 CAS#: 871026-44-7 Chemical Formula: $C_{26}H_{25}ClF_3N_5O_3$ Exact Mass: 547.1598 Molecular Weight: 547.96	
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:
TAK-285 is a novel dual erbB protein kinase inhibitor that specifically targets human epidermal growth factor receptor (EGFR) and HER2. Methods: TAK-285 is currently being developed by Takeda. TAK-285 was found to be well tolerate in Phase I trials. Absorption of TAK-285 was rapid after oral dosing, and plasma exposure at steady-state increased in a dose-proportional fashion for doses ranging from 50 to 300 mg b.i.d. A partial response was observed for one patient with parotid cancer who received 300 mg b.i.d. The toxicity profile and PK properties of oral TAK-285 warrant further evaluation.

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	80.0	146.0
Ethanol	54.0	98.55

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.82 mL	9.12 mL	18.25 mL
5 mM	0.36 mL	1.82 mL	3.65 mL
10 mM	0.18 mL	0.91 mL	1.82 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. Nakayama A, Takagi S, Yusa T, Yaguchi M, Hayashi A, Tamura T, Kawakita Y, Ishikawa T, Ohta Y. Antitumor Activity of TAK-285, an Investigational, Non-Pgp Substrate HER2/EGFR Kinase Inhibitor, in Cultured Tumor Cells, Mouse and Rat Xenograft Tumors, and in an HER2-Positive Brain Metastasis Model. J Cancer. 2013 Aug 16;4(7):557-65. doi: 10.7150/jca.6689. PMID: 23983820; PMCID: PMC3753530.

In vivo study

1. Nakayama A, Takagi S, Yusa T, Yaguchi M, Hayashi A, Tamura T, Kawakita Y, Ishikawa T, Ohta Y. Antitumor Activity of TAK-285, an Investigational, Non-Pgp Substrate HER2/EGFR Kinase Inhibitor, in Cultured Tumor Cells, Mouse and Rat Xenograft Tumors, and in an HER2-Positive Brain Metastasis Model. J Cancer. 2013 Aug 16;4(7):557-65. doi: 10.7150/jca.6689. PMID: 23983820; PMCID: PMC3753530.

7. Bioactivity
Biological target: TAK-285 is a HER2 and EGFR(HER1) inhibitor with IC50 of 17 nM and 23 nM, respectively.

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In vitro activity

TAK-285 had a growth inhibitory effect in multiple cell lines. Sensitivities of various cell lines to growth inhibition by TAK-285 are shown in Table 1. In general, cells with higher expression of HER2 were more sensitive to TAK-285, but A-431 cells, which overexpress EGFR, were also sensitive to TAK-285. The IC50 for BT-474 cells was 0.017 μmol/L compared with 1.1 and 20 μmol/L in A-431 and MRC-5 cells which do not overexpress HER2. In other experiments, TAK-285 inhibited HER2 phosphorylation in BT-474 cells with IC50 values of 0.0093 μmol/L (95% CI 0.0065, 0.012). TAK-285 also inhibited Akt and MAPK phosphorylation in a dose-dependent manner, with IC50 values of 0.015 μmol/L (95% CI: 0.011, 0.018) and <0.0063 μmol/L, respectively. In A-431 cells, the IC50 value for TAK-285 inhibition of EGFR phosphorylation was 0.053 μmol/L (95% CI 0.040, 0.069).

Reference: 2013 Aug 16;4(7):557-65. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3753530/

In vivo activity

The tumor growth inhibitory effect of TAK-285 was tested in a murine intracranial injection model of brain metastases using BT-474-derived cerebral xenografts that resulted in highly reproducible tumor growth in a defined intracranial region (Figure 5A). For these experiments, a line of luciferase-detectable BT-474 cells (BTLUC) that allowed non-invasive monitoring of intracranial xenograft growth (Figure 5B) was developed. BTLUC cells possessed highly activated HER2 with phosphorylation comparable to parental BT-474 cells (Figure 5C) and sensitivity to TAK-285 with IC50 value of 90 nmol/L (95% CI: 76-107nmol/L). TAK-285 inhibited intracranial xenograft growth with T/C values of 44% on day 41 (Figure 6, P = 0.011 vs control).

Reference: 2013 Aug 16;4(7):557-65. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3753530/