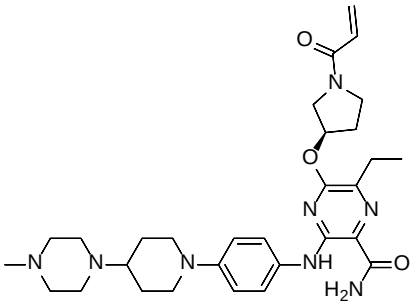
Product data sheet

MedKoo Cat#: 206137 Name: Naquotinib free base CAS: 1448232-80-1 (free base) Chemical Formula: $C_{30}H_{42}N_8O_3$ Exact Mass: 562.338 Molecular Weight: 562.719	
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:

Naquotinib, also known as ASP8273, is an orally available, irreversible, third-generation, mutant-selective, epidermal growth factor receptor (EGFR) inhibitor, with potential antineoplastic activity. Upon oral administration, ASP8273 covalently binds to and inhibits the activity of mutant forms of EGFR, including the T790M EGFR mutant, thereby preventing EGFR-mediated signaling. This may both induce cell death and inhibit tumor growth in EGFR-overexpressing tumor cells. EGFR, a receptor tyrosine kinase mutated in many tumor cell types, plays a key role in tumor cell proliferation and tumor vascularization. ASP8273 preferentially inhibits mutated forms of EGFR including T790M, a secondarily acquired resistance mutation, and may have therapeutic benefits in tumors with T790M-mediated resistance when compared to other EGFR tyrosine kinase inhibitors.

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	30.0	53.31
DMSO	2.0	3.55
Ethanol	30.0	55.31

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	1.78 mL	8.89 mL	17.77 mL
5 mM	0.36 mL	1.78 mL	3.55 mL
10 mM	0.18 mL	0.89 mL	1.78 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. Tanaka H, Kaneko N, Sakagami H, Matsuya T, Hiramoto M, Yamanaka Y, Mori M, Koshio H, Hirano M, Takeuchi M. Naquotinib exerts antitumor activity in activated B-cell-like diffuse large B-cell lymphoma. Leuk Res. 2020 Jan;88:106286. doi: 10.1016/j.leukres.2019.106286. Epub 2019 Dec 10. PMID: 31865062.
2. Hirano T, Yasuda H, Hamamoto J, Nukaga S, Masuzawa K, Kawada I, Naoki K, Niimi T, Mimasu S, Sakagami H, Soejima K, Betsuyaku T. Pharmacological and Structural Characterizations of Naquotinib, a Novel Third-Generation EGFR Tyrosine Kinase Inhibitor, in EGFR-Mutated Non-Small Cell Lung Cancer. Mol Cancer Ther. 2018 Apr;17(4):740-750. doi: 10.1158/1535-7163.MCT-17-1033. Epub 2018 Feb 21. PMID: 29467275.

In vivo study

Product data sheet

1. Tanaka H, Sakagami H, Kaneko N, Konagai S, Yamamoto H, Matsuya T, Yuri M, Yamanaka Y, Mori M, Takeuchi M, Koshio H, Hirano M, Kuromitsu S. Mutant-Selective Irreversible EGFR Inhibitor, Naquotinib, Inhibits Tumor Growth in NSCLC Models with EGFR-Activating Mutations, T790M Mutation, and AXL Overexpression. Mol Cancer Ther. 2019 Aug;18(8):1366-1373. doi: 10.1158/1535-7163.MCT-18-0976. Epub 2019 May 15. PMID: 31092564.

7. Bioactivity

Biological target:

Naquotinib (ASP8273) is an orally available, mutant-selective and irreversible EGFR inhibitor; with IC_{50}s of 8-33 nM toward EGFR mutants and 230 nM for EGFR.

In vitro activity

The efficacy of naquotinib in cells with L858R, exon 19 deletion and exon 19 deletion+T790M was comparable with that of osimertinib. Interestingly, naquotinib was more potent than osimertinib for L858R+T790M. Additionally, naquotinib and osimertinib had comparable efficacy and a wide therapeutic window for cells with EGFR exon 20 insertions.

Reference: Mol Cancer Ther. 2018 Apr;17(4):740-750. https://pubmed.ncbi.nlm.nih.gov/29467275/

In vivo activity

In in vivo murine xenograft models using cell lines and a patient-derived xenograft model, naquotinib induced tumor regression of NSCLC with EGFR-activating mutations with or without T790M resistance mutation, whereas it did not significantly inhibit WT EGFR signaling in skin. Furthermore, naquotinib suppressed tumor recurrence during the treatment period of 90 days. In addition, unlike erlotinib and osimertinib, naquotinib inhibited the phosphorylation of AXL and showed antitumor activity against PC-9 cells overexpressing AXL in vitro and in vivo.

Reference: Mol Cancer Ther. 2019 Aug;18(8):1366-1373. https://pubmed.ncbi.nlm.nih.gov/31092564/