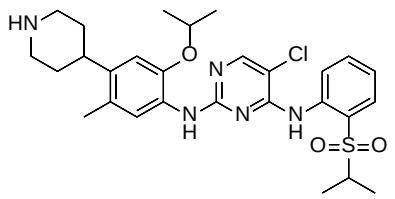
Product data sheet

MedKoo Cat#: 205511 Name: Ceritinib free base CAS#: 1032900-25-6 (free base) Chemical Formula: $C_{28}H_{36}ClN_5O_3S$ Exact Mass: 557.2227 Molecular Weight: 558.14	
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:
Ceritinib, also known as LDK378, is a selective inhibitor of ALK1, a target found in metastatic non-small cell lung cancer (NSCLC). In Phase I trials, LDK378 showed a marked clinical response in 78 patients with anaplastic lymphoma kinase positive (ALK+) metastatic non-small cell lung cancer (NSCLC) who had progressed during or after crizotinib therapy or had not been previously treated with crizotinib. LDK378 blocks the ALK protein and stops it sending growth signals to cancer cells, which may stop them growing. Ceritinib was approved in April 2014.

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	2.79	5.0

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.79 mL	8.96 mL	17.92 mL
5 mM	0.36 mL	1.79 mL	3.58 mL
10 mM	0.18 mL	0.90 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. Friboulet L, Li N, Katayama R, Lee CC, Gainor JF, Crystal AS, Michellys PY, Awad MM, Yanagitani N, Kim S, Pferdekamper AC, Li J, Kasibhatla S, Sun F, Sun X, Hua S, McNamara P, Mahmood S, Lockerman EL, Fujita N, Nishio M, Harris JL, Shaw AT, Engelman JA. The ALK inhibitor ceritinib overcomes crizotinib resistance in non-small cell lung cancer. Cancer Discov. 2014 Jun;4(6):662-673. doi: 10.1158/2159-8290.CD-13-0846. Epub 2014 Mar 27. PMID: 24675041; PMCID: PMC4068971.

In vivo study

1. Friboulet L, Li N, Katayama R, Lee CC, Gainor JF, Crystal AS, Michellys PY, Awad MM, Yanagitani N, Kim S, Pferdekamper AC, Li J, Kasibhatla S, Sun F, Sun X, Hua S, McNamara P, Mahmood S, Lockerman EL, Fujita N, Nishio M, Harris JL, Shaw AT, Engelman JA. The ALK inhibitor ceritinib overcomes crizotinib resistance in non-small cell lung cancer. Cancer Discov. 2014 Jun;4(6):662-673. doi: 10.1158/2159-8290.CD-13-0846. Epub 2014 Mar 27. PMID: 24675041; PMCID: PMC4068971.

7. Bioactivity
Biological target: Ceritinib (LDK378) is a selective, ATP-competitive ALK tyrosine kinase inhibitor with an IC50 of 200 pM.

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In vitro activity

Interrogation of in vitro models of acquired resistance to crizotinib, including cell lines established from biopsies of crizotinib-resistant NSCLC patients, revealed that ceritinib potently overcomes crizotinib resistance mutations. In particular, ceritinib effectively inhibits ALK harboring L1196M, G1269A, I1171T and S1206Y mutations, and a co-crystal of ceritinib bound to ALK provides structural bases for this increased potency. However, ceritinib did not overcome two crizotinib-resistant ALK mutations, G1202R and F1174C.

Reference: Cancer Discov. 2014 Jun;4(6):662-673. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4068971/

In vivo activity

The efficacy of ceritinib was tested against crizotinib-resistant H2228 xenograft tumor models as well as one of the resistance models that did not harbor a resistance mutation nor ALK amplification. While each was resistant to crizotinib at 100 mg/kg, ceritinib suppressed tumor growth in multiple resistance models (Fig.5A, B, C and D). In the wild-type and I1171T resistant models, ceritinib demonstrated impressive anti-tumor activity, while it was less active in the C1156Y resistant model and was inactive against the G1202R resistant model. This data is consistent with the Ba/F3 models in which ceritinib was more potent against I1171T than the C1156Y and G1202R mutants (Fig. 4A). This data provides evidence that ceritinib can overcome resistance in vivo, especially in tumors harboring wild-type, L1196M or I1171T ALK fusion genes.

Reference: Cancer Discov. 2014 Jun;4(6):662-673. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4068971/