# Product data sheet

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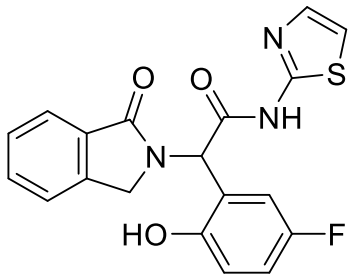
|---|---|
| MedKoo Cat#: 406836<br>Name: EAI045<br>CAS#: 1942114-09-1<br>Chemical Formula: $C_{19}H_{14}FN_3O_3S$<br>Exact Mass: 383.074<br>Molecular Weight: 383.3974 |  |
| Product supplied as: | Powder |
| Purity (by HPLC): | ≥ 98% |
| Shipping conditions | Ambient temperature |
| Storage conditions: | Powder: -20°C 3 years; 4°C 2 years. |
| | In solvent: -80°C 3 months; -20°C 2 weeks. |

**1. Product description:**
EAI045 ia a potent and selective EGFR inhbitor. EAI045 targets selected drug-resistant EGFR mutants but spares the wild-type receptor. EAI045 inhibits L858R/T790M-mutant EGFR with low-nanomolar potency in biochemical assays.

**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 | 76 | 198.23 |

**4. Stock solution preparation table:**

| Concentration / Solvent Volume / Mass | 1 mg | 5 mg | 10 mg |
|---|---|---|---|
| 1 mM | 2.61 mL | 13.04 mL | 26.08 mL |
| 5 mM | 0.52 mL | 2.61 mL | 5.22 mL |
| 10 mM | 0.26 mL | 1.30 mL | 2.61 mL |
| 50 mM | 0.05 mL | 0.26 mL | 0.52 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. Wang S, Song Y, Liu D. EAI045: The fourth-generation EGFR inhibitor overcoming T790M and C797S resistance. Cancer Lett. 2017 Jan 28;385:51-54. doi: 10.1016/j.canlet.2016.11.008. Epub 2016 Nov 10. PMID: 27840244.

2. Wang S, Tsui ST, Liu C, Song Y, Liu D. EGFR C797S mutation mediates resistance to third-generation inhibitors in T790M-positive non-small cell lung cancer. J Hematol Oncol. 2016 Jul 22;9(1):59. doi: 10.1186/s13045-016-0290-1. PMID: 27448564; PMCID: PMC4957905.

In vivo study

1. Wang S, Song Y, Liu D. EAI045: The fourth-generation EGFR inhibitor overcoming T790M and C797S resistance. Cancer Lett. 2017 Jan 28;385:51-54. doi: 10.1016/j.canlet.2016.11.008. Epub 2016 Nov 10. PMID: 27840244.

2. Jia Y, Yun CH, Park E, Ercan D, Manuia M, Juarez J, Xu C, Rhee K, Chen T, Zhang H, Palakurthi S, Jang J, Lelais G, DiDonato M, Bursulaya B, Michellys PY, Epple R, Marsilje TH, McNeill M, Lu W, Harris J, Bender S, Wong KK, Jänne PA, Eck MJ. Overcoming EGFR(T790M) and EGFR(C797S) resistance with mutant-selective allosteric inhibitors. Nature. 2016 Jun 2;534(7605):129-32. doi: 10.1038/nature17960. Epub 2016 May 25. PMID: 27251290; PMCID: PMC4929832.

**7. Bioactivity**

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Biological target:

EAI045 is an allosteric and the fourth-generation inhibitor of mutant EGFR with IC50s of 1.9, 0.019, 0.19 and 0.002 μM for EGFR, EGFRL858R, EGFRT790M and EGFRL858R/T790M at 10 μM ATP, respectively.

In vitro activity

In L858R/T790M-mutant NSCLC cell line H1975 cells, EAI045 decreased but did not completely abolish the EGFR auto-phosphorylation. In stably transfected NIH-3T3 cells harboring the L858R/T790M EGFR mutant, EAI045 showed the same activity. In L858R-mutant H3255 cells, EAI045 exhibited moderate activity. In the HaCaT cells, a keratinocyte cell line with wild-type EGFR, EAI045 did not show any activity of inhibiting EGFR phosphorylation. These again confirmed the selectivity of EAI045 for mutant EGFR. Since dimerization of EGFR is required for its activation, these investigators hypothesized that the allosteric inhibitor was inactive for those asymmetric dimers/dimers between wild-type and mutant EGFR peptides. The investigators confirmed that EAI045 was markedly more active in dimerization-defective EGFR mutants. When combined with cetuximab, a monoclonal antibody that can block EGFR dimerization by preventing EGF ligand binding, EAI045 markedly inhibited the proliferation of Ba/F3 cells bearing L858R/T790M mutation. These in vitro studies proved that EAI045 is active and selective for T790M- harboring EGFR mutants that are in a monomer state.

Reference: Cancer Lett. 2017 Jan 28;385:51-54. https://linkinghub.elsevier.com/retrieve/pii/S0304-3835(16)30686-3

In vivo activity

In a genetically engineered mouse model of L858R/T790M-mutant-driven lung cancer, the efficacy of EAI045 was tested alone and in combination with cetuximab. Remarkable tumor regression was observed in L858R/T790M-mutant mice treated with the combination of EAI045 and cetuximab. No response was seen in those mice treated with EAI045 alone. The same effect was seen in both L858R/T790M/C797S- engineered Ba/F3 cells and in mice carrying the L858R/T790M/C797S tumor xenografts. These assays clearly showed that EAI045 can overcome resistance from acquired T790M and C797S mutations.

Reference: Cancer Lett. 2017 Jan 28;385:51-54. https://linkinghub.elsevier.com/retrieve/pii/S0304-3835(16)30686-3