# Product data sheet

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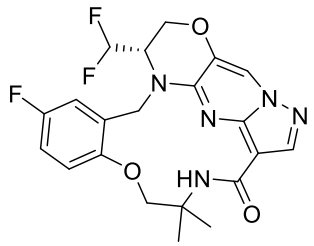
|---|---|
| MedKoo Cat#: 556040<br>Name: TPX-0131<br>CAS#: 2648641-36-3<br>Chemical Formula: $C_{21}H_{20}F_3N_5O_3$<br>Exact Mass: 447.1518<br>Molecular Weight: 447.4182 |  |
| Product supplied as: | Powder |
| Purity (by HPLC): | ≥ 98% |
| Shipping conditions | Ambient temperature |
| Storage conditions: | Powder: -20°C 3 years; 4°C 2 years. |
| | In solvent: -80°C 3 months; -20°C 2 weeks. |

**1. Product description:**

TPX-0131 is a Potent CNS-penetrant, Next-generation Inhibitor of Wild-type ALK and ALK-resistant Mutations. In cellular assays, TPX-0131 was more potent than all five approved ALK inhibitors against WT ALK and many types of ALK resistance mutations, e.g., G1202R, L1196M, and compound mutations. In biochemical assays, TPX-0131 potently inhibited (IC50 <10 nmol/L) WT ALK and 26 ALK mutants (single and compound mutations). TPX-0131, but not lorlatinib, caused complete tumor regression in ALK (G1202R) and ALK compound mutation-dependent xenograft models. Following repeat oral administration of TPX-0131 to rats, brain levels of TPX-0131 were approximately 66% of those observed in plasma.

**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 | 25.0 | 55.88 |

**4. Stock solution preparation table:**

| Concentration / Solvent Volume / Mass | 1 mg | 5 mg | 10 mg |
|---|---|---|---|
| 1 mM | 2.24 mL | 11.18 mL | 22.35 mL |
| 5 mM | 0.45 mL | 2.24 mL | 4.47 mL |
| 10 mM | 0.22 mL | 1.12 mL | 2.24 mL |
| 50 mM | 0.04 mL | 0.22 mL | 0.45 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. Murray BW, Zhai D, Deng W, Zhang X, Ung J, Nguyen V, Zhang H, Barrera M, Parra A, Cowell J, Lee DJ, Aloysius H, Rogers E. TPX-0131, a Potent CNS-penetrant, Next-generation Inhibitor of Wild-type ALK and ALK-resistant Mutations. Mol Cancer Ther. 2021 Sep;20(9):1499-1507. doi: 10.1158/1535-7163.MCT-21-0221. Epub 2021 Jun 22. PMID: 34158340.

In vivo study

1. Murray BW, Zhai D, Deng W, Zhang X, Ung J, Nguyen V, Zhang H, Barrera M, Parra A, Cowell J, Lee DJ, Aloysius H, Rogers E. TPX-0131, a Potent CNS-penetrant, Next-generation Inhibitor of Wild-type ALK and ALK-resistant Mutations. Mol Cancer Ther. 2021 Sep;20(9):1499-1507. doi: 10.1158/1535-7163.MCT-21-0221. Epub 2021 Jun 22. PMID: 34158340.

**7. Bioactivity**

Biological target:

TPX-0131 is a potent, selective, CNS-penetrant inhibitor of wild-type ALK (IC50 of 1.4 nM) and ALK-resistant mutation, e.g. G1202R (IC50 of 0.3 nM), L1196M (IC50 of 0.3 nM) that has strong antitumor activities.

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In vitro activity

TPX-0131 suppressed autophosphorylation of Tyr1604 and Tyr1282/1283 residues of ALK oncogenic fusion proteins in engineered stable cell lines expressing WT or mutant ALK fusion proteins. TPX-0131 exhibited comparable activity to lorlatinib in suppressing WT EML4-ALK phosphorylation with an IC50 value of approximately 3 to 10 nmol/L. TPX-0131 was a potent inhibitor of ALK autophosphorylation in Ba/F3 cells expressing EML4-ALK G1202R solvent front, EML4-ALK G1202R/L1196M, or EML4-ALK G1202R/L1198F mutations, with IC50 values of approximately 3 to 10 nmol/L. In conclusion, TPX-0131 demonstrates potent inhibition of both single and compound EML4-ALK resistance mutations by TPX-0131.

Reference: Mol Cancer Ther. 2021 Sep;20(9):1499-1507. https://pubmed.ncbi.nlm.nih.gov/34158340/

In vivo activity

The correlation of inhibition of ALK phosphorylation (Tyr1282/1283) was evaluated as a function of TPX-0131 plasma exposure analysis using the Ba/F3 CDX model harboring the EML4-ALK fusion with the G1202R/L1196M compound mutation. For 2 and 5 mg/kg doses of TPX-0131, near complete suppression of phospho-ALK (92%–95%) was observed. However, 12 hours after single-dose TPX-0131 administration, the level phospho-ALK suppression was reduced (0%–63%) consistent with the use of a BID dosing regimen in mouse models. TPX-0131 exhibited more than 90% phosphorylation inhibition of EML4-ALK G1202R/L1196M fusion at a mean free plasma concentration of 19.5 nmol/L. Tumor growth inhibition correlates with TPX-0131 exposure and suppression of ALK phosphorylation. Taken together, TPX-0131 demonstrated marked antitumor effects in Ba/F3 CDX models of ALK resistance mutations such as the G1202R solvent front mutation, the G1202R/L1198F compound mutation, and the gatekeeper/solvent front compound mutation G1202R/L1196M.

Reference: Mol Cancer Ther. 2021 Sep;20(9):1499-1507. https://pubmed.ncbi.nlm.nih.gov/34158340/