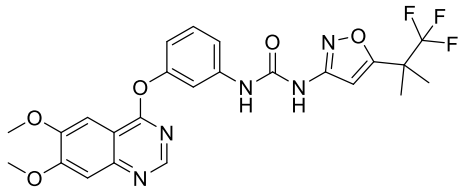
Product data sheet

MedKoo Cat#: 205903 Name: RXDX-105 (CEP-32496) CAS#: 1188910-76-0 (free base) Chemical Formula: $C_{24}H_{22}F_3N_5O_5$ Exact Mass: 517.1573 Molecular Weight: 517.47	
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:
RXDX-105, also known as Agerafenib, CEP-32496 and AC013773, is an orally available v-raf murine sarcoma viral oncogene homolog B1 (B-raf) serine/threonine protein kinase inhibitor with potential antineoplastic activity.

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	10	19.32
DMSO	20	38.65
Ethanol	2	3.86

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	1.93 mL	9.66 mL	19.32 mL
5 mM	0.39 mL	1.93 mL	3.86 mL
10 mM	0.19 mL	0.97 mL	1.93 mL
50 mM	0.04 mL	0.19 mL	0.39 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. Flynn SM, Lesperance J, Macias A, Phanhthilath N, Paul MR, Kim JW, Tamayo P, Zage PE. The multikinase inhibitor RXDX-105 is effective against neuroblastoma in vitro and in vivo. Oncotarget. 2019 Oct 29;10(59):6323-6333. doi: 10.18632/oncotarget.27259. PMID: 31695841; PMCID: PMC6824878.
2. James J, Ruggeri B, Armstrong RC, Rowbottom MW, Jones-Bolin S, Gunawardane RN, Dobrzanski P, Gardner MF, Zhao H, Cramer MD, Hunter K, Nepomuceno RR, Cheng M, Gitnick D, Yazdanian M, Insko DE, Ator MA, Apuy JL, Faraoni R, Dorsey BD, Williams M, Bhagwat SS, Holladay MW. CEP-32496: a novel orally active BRAF(V600E) inhibitor with selective cellular and in vivo antitumor activity. Mol Cancer Ther. 2012 Apr;11(4):930-41. doi: 10.1158/1535-7163.MCT-11-0645. Epub 2012 Feb 7. PMID: 22319199.

In vivo study

1. Jiang C, Xie L, Zhang Y, Fujinaga M, Mori W, Kurihara Y, Yamasaki T, Wang F, Zhang MR. Pharmacokinetic Evaluation of [11C]CEP-32496 in Nude Mice Bearing BRAFV600E Mutation-Induced Melanomas. Mol Imaging. 2018 Jan-Dec;17:1536012118795952. doi: 10.1177/1536012118795952. PMID: 30251592; PMCID: PMC6156206.

2. Shimoda Y, Yui J, Fujinaga M, Xie L, Kumata K, Ogawa M, Yamasaki T, Hatori A, Kawamura K, Zhang MR. [(11)C-carbonyl]CEP-32496: radiosynthesis, biodistribution and PET study of brain uptake in P-gp/BCRP knockout mice. Bioorg Med Chem Lett. 2014 Aug 1;24(15):3574-7. doi: 10.1016/j.bmcl.2014.05.045. Epub 2014 Jun 2. PMID: 24930831.

7. Bioactivity

Biological target:

RXDX-105 specifically and selectively inhibits the activity of the mutated form (V600E) of B-raf kinase with a Kd of 14 nM. This inhibits the activation of the RAF/mitogen-activated protein kinase kinase (MEK)/extracellular signal-related kinase (ERK) signaling pathway and may result in a decrease in the proliferation of tumor cells expressing the mutated B-raf gene.

In vitro activity

Treatment with RXDX-105 resulted in a substantial reduction in neuroblastoma cell viability and proliferation. It effectively inhibited key molecular signaling pathways, including the phosphorylation of RET, MEK, and ERK kinases, suggesting its potential to disrupt critical cellular processes. RXDX-105 induced both apoptosis and cell cycle arrest in neuroblastoma cells.

Reference: Oncotarget. 2019 Oct 29; 10(59): 6323–6333. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6824878/

In vivo activity

Carbon-11-labeled RXDX-105 ([11C]RXDX-105) demonstrated high binding affinity for BRAFV600E-positive A375 melanoma cells and densely accumulated in tumor tissue sections in mice with the BRAFV600E mutation. There was a slow but continuous accumulation of [11C]RXDX-105 in melanoma tumors. [11C]RXDX-105 has high stability in plasma. These findings suggest that [11C]RXDX-105 could be a potential candidate for noninvasive personalized diagnostic applications.

Reference: Mol Imaging. 2018 Jan-Dec;17:1536012118795952. https://pubmed.ncbi.nlm.nih.gov/30251592/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.