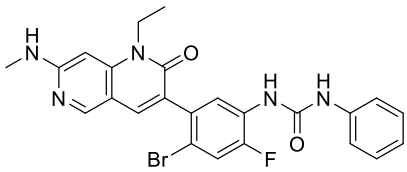
Product data sheet

MedKoo Cat#: 206497 Name: Ripretinib free base CAS#: 1442472-39-0 (free base) Chemical Formula: $C_{24}H_{21}BrFN_5O_2$ Exact Mass: 509.0863 Molecular Weight: 510.37	
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:
Ripretinib, also known as DCC-2618, is a potent, orally active and selective KIT/PDGFR inhibitor with potential antineoplastic activity. DCC-2618 targets and binds to both wild-type and mutant forms of KIT and PDGFRa specifically at their switch pocket binding sites, thereby preventing the switch from inactive to active conformations of these kinases and inactivating their wild-type and mutant forms. In May 2020, FDA Approves Qinlock (ripretinib) for the Treatment of Fourth-Line Gastrointestinal Stromal Tumor

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	49.0

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.96 mL	9.80 mL	19.59 mL
5 mM	0.39 mL	1.96 mL	3.92 mL
10 mM	0.20 mL	0.98 mL	1.96 mL
50 mM	0.04 mL	0.20 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. Smith BD, Kaufman MD, Lu WP, Gupta A, Leary CB, Wise SC, Rutkoski TJ, Ahn YM, Al-Ani G, Bulfer SL, Caldwell TM, Chun L, Ensinger CL, Hood MM, McKinley A, Patt WC, Ruiz-Soto R, Su Y, Telikepalli H, Town A, Turner BA, Vogeti L, Vogeti S, Yates K, Janku F, Abdul Razak AR, Rosen O, Heinrich MC, Flynn DL. Ripretinib (DCC-2618) Is a Switch Control Kinase Inhibitor of a Broad Spectrum of Oncogenic and Drug-Resistant KIT and PDGFRA Variants. Cancer Cell. 2019 May 13;35(5):738-751.e9. doi: 10.1016/j.ccell.2019.04.006. PMID: 31085175.
2. Schneeweiss M, Peter B, Bibi S, Eisenwort G, Smiljkovic D, Blatt K, Jawhar M, Berger D, Stefanzl G, Herndlhofer S, Greiner G, Hoermann G, Hadzijusufovic E, Gleixner KV, Bettelheim P, Geissler K, Sperr WR, Reiter A, Arock M, Valent P. The KIT and PDGFRA switch-control inhibitor DCC-2618 blocks growth and survival of multiple neoplastic cell types in advanced mastocytosis. Haematologica. 2018 May;103(5):799-809. doi: 10.3324/haematol.2017.179895. Epub 2018 Feb 8. PMID: 29439183; PMCID: PMC5927976.

In vivo study

1. Smith BD, Kaufman MD, Lu WP, Gupta A, Leary CB, Wise SC, Rutkoski TJ, Ahn YM, Al-Ani G, Bulfer SL, Caldwell TM, Chun L, Ensinger CL, Hood MM, McKinley A, Patt WC, Ruiz-Soto R, Su Y, Telikepalli H, Town A, Turner BA, Vogeti L, Vogeti S, Yates K, Janku F, Abdul Razak AR, Rosen O, Heinrich MC, Flynn DL. Ripretinib (DCC-2618) Is a Switch Control Kinase Inhibitor of a

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Broad Spectrum of Oncogenic and Drug-Resistant KIT and PDGFRA Variants. Cancer Cell. 2019 May 13;35(5):738-751.e9. doi: 10.1016/j.ccell.2019.04.006. PMID: 31085175.

7. Bioactivity

Biological target:

Ripretinib (DCC-2618) is a KIT and PDGFRA switch-control inhibitor.

In vitro activity

Based on this safety profile, ripretinib was formulated into a mouse diet to achieve approximate levels of 100 and 25 mg/kg/day in mouse efficacy studies. In the GIST T1 model treated with ripretinib, significant tumor regression was observed at both doses (Figure 3A). At the high dose, 6/10 mice had complete tumor regression, with the remaining 4/10 mice having partial tumor regression during the dosing period. At the low dose, 2/10 mice had complete tumor regression, and 6/10 had partial tumor regression. Tumors exhibited slow regrowth after the end of the dosing period. Survival to study endpoint (day 68) was 100% for ripretinib-treated mice and 25% for vehicle-treated mice (Figure 3B). Body weight changes for ripretinib-treated groups were similar to vehicle (Figure S4D).

Reference: Cancer Cell. 2019 May 13;35(5):738-751.e9. https://www.cell.com/cancer-cell/fulltext/S1535-6108(19)30201-6

In vivo activity

DCC-2618 and its active metabolite, DP-5439 were found to inhibit 3H-thymidine uptake and thus proliferation in a dose-dependent manner in all MC lines tested, with slightly lower IC50 values obtained in HMC-1.1 cells lacking KIT D816V and ROSAKIT WT cells compared to the KIT D816V-positive cell lines HMC-1.2 and ROSAKIT D816V (Figure 1A and Table 2). In addition, DCC-2618 and DP-5439 were found to inhibit proliferation of ROSAKIT K509I cells with lower IC50 values (DCC-2618, IC50: 34±10 nM) compared to ROSAKIT D816V cells (Figure 1A). Unexpectedly, DCC-2618 and its metabolite also produced growth-inhibition in the multi-resistant MC lines MCPV-1.1, MCPV-1.2, MCPV-1.3 and MCPV-1.4 (Figure 1B and Table 2). Finally, DCC-2618 and DP- 5439 induced dose-dependent inhibition of growth of primary neoplastic bone marrow cells obtained from patients suffering from various forms of SM, including ASM and MCL (Figure 1C, Table 1). Interestingly, the effects of DCC-2618 on primary neoplastic BM cells and the related IC50 values obtained in different SM variants were comparable (Figure 1C, Table 1).

Reference: Haematologica. 2018 May; 103(5): 799–809. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5927976/

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.