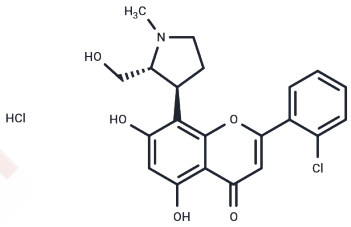
# Data Sheet (Cat.No.T6924)

TargetMol

## Riviciclib hydrochloride

### Chemical Properties



CAS No. : 920113-03-7

Formula: C21H20ClNO5·HCl

Molecular Weight: 438.3

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

### Biological Description

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| Description | Riviciclib hydrochloride (P276-00) is a novel inhibitor of CDK1, CDK4, and CDK9, with IC50 values of 79 nM, 63 nM, and 20 nM, respectively, currently in Phase 2/3. |
| Targets(IC50) | Apoptosis,CDK |
| In vitro | Riviciclib shows 40-fold selectivity toward Cdk4-D1, compared with Cdk2-E[1]. It shows potent antiproliferative effects against various human cancer cell lines, including HCT-116, U2OS, H-460, HL-60, HT-29, SiHa, MCF-7, Colo-205, SW-480, PC-3, Caco2, T-24 with an IC50 ranging from 300 to 800 nmol/L, and is found to be highly selective for cancer cells as compared with normal fibroblast cells[1]. Riviciclib can down-regulate cyclin D1 and Cdk4 in an ATP- competitive manner and decrease Cdk4-specific pRb Ser780 phosphorylation. Riviciclib also induces apoptosis by actving cellular caspase-3 activity and DNA ladder formation[1]. |
| In vivo | Riviciclib, administered i.p. at 50 mg/kg daily for 20 treatments can significantly induce growth inhibition of murine colon cancer (CA-51). However, in murine lung carcinoma model (Lewis lung), an increased dose of 60 mg/kg (30 mg/kg twice daily) administered every alternate day i.p. for 7 treatments shows significant inhibition in the growth[2]. And it also inhibit the growth of human colon carcinoma HCT-116 xenograft and human non-small cell lung carcinoma H-460 xenograft[2]. Efficacy Studies show its maximum tolerated dose is 78 mg/kg/d[2]. |
| Kinase Assay | Cdk4-D1/Cdk2-E enzyme assay: The Cdk4-D1/Cdk2-E enzyme assay is run in 96-well format using Millipore Multiscreen filtration plates. All assay steps are done in a single filter plate. The filtration wells are prewetted with 100 µL of kinase buffer [50 mmol/L HEPES (pH, 7.5), 10 mmol/L MgCl2, 1 mmol/L EGTA], and then the solution is removed by vacuum. With filter plate on vacuum manifold, 50 µL GST-Rb bound to GSH-Sepharose beads in kinase buffer (0.5 µg GST-Rb/50 µL) is added to each well, and vacuum is applied to the filter plate. About 25 µL of a reaction mix containing ATP (cold + hot) and 4× phosphatase inhibitor mix (40 µMol/L unlabeled ATP, 10 µCi/mL γ32P-ATP, 40 mmol/L h-glycerophosphate, 4 mmol/L DTT, 0.4 mmol/L NaF, 0.4 mmol/L sodium orthovanadate) diluted in kinase buffer is added to each well. The test compound (4×final concentration in kinase buffer) or kinase buffer alone (control) is then added in an additional 25 µL volume. To each well, 50 µL (100 ng) of human Cdk4-D1/Cdk2-E enzyme in kinase buffer is added to initiate the reaction, which is allowed to continue for 30 min at 30°C. When the reaction is completed, vacuum is applied again, and the |

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| Kinase Assay | plate is washed with the TNEN buffer [20 mmol/L Tris (pH, 8.0), 100 mmol/L NaCl, 1 mmol/L EDTA, 0.5% nonidet-P40] thrice; the filter plate is air-dried and is placed in a Multiscreen adapter plate. Packard Microscint-O cocktail (30 μL) is added, and the plate is covered with a Top-Seal A film. Quantitation of 32P-GST-Rb in 96-well filter plates is carried out by Top Count scintillation counter. All compounds are tested initially at 1 μMol/L concentration. Compounds showing more than or equal to 50% inhibition are further profiled for IC50 determination. |
| Cell Research | The cells are seeded at a density of 3,000-5,000 cells per well, depending on cell type in 180 μL of culture medium in 96-well plate and incubated overnight to allow the cells to adhere. Varying concentrations of compounds are added to the wells and incubated for 48 h at 37°C. 3H-thymidine (0.25 μCi) is added to each well, and incorporation of the radiolabel is allowed to proceed for 5 to 7 h. Following this incubation, cells are harvested onto GF/B unifilter plates using a Packard Filtermate Universal harvester, and the plates are counted in a Packard Top Count 96-well liquid scintillation counter. (Only for Reference) |

## Solubility Information

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| Solubility | Ethanol: 7 mg/mL (15.97 mM),Sonication is recommended.<br>DMSO: 50 mg/mL (114.08 mM),Sonication is recommended.<br>H2O: 81 mg/mL (184.8 mM),Sonication is recommended.<br>(< 1 mg/ml refers to the product slightly soluble or insoluble) |
| In vivo Formulation | 10% DMSO+90% Saline: 5 mg/mL (11.41 mM),Solution.<br>10% DMSO+40% PEG300+5% Tween 80+45% Saline: 3.3 mg/mL (7.53 mM),Sonication is recommended.<br>*Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.* |

Preparing Stock Solutions

| | 1mg | 5mg | 10mg |
|---|---|---|---|
| 1 mM | 2.2815 mL | 11.4077 mL | 22.8154 mL |
| 5 mM | 0.4563 mL | 2.2815 mL | 4.5631 mL |
| 10 mM | 0.2282 mL | 1.1408 mL | 2.2815 mL |
| 50 mM | 0.0456 mL | 0.2282 mL | 0.4563 mL |

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Joshi KS, et al. Mol Cancer Ther, 2007, 6(3), 918-925.
Joshi KS, et al. Mol Cancer Ther, 2007, 6(3), 926-934.

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