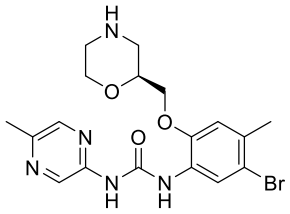
Product data sheet

MedKoo Cat#: 201794 Name: Rabusertib (LY2603618) CAS#: 911222-45-2 Chemical Formula: $C_{18}H_{22}BrN_5O_3$ Exact Mass: 435.0906 Molecular Weight: 436.3	
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:

Rabusertib, also known as LY2603618, is a n inhibitor of the cell cycle checkpoint kinase 2 (chk2) with potential chemopotentiating activity. Rabusertib binds to and inhibits the activity of chk2, which may prevent the repair of DNA caused by DNA-damaging agents, thus potentiating the antitumor efficacies of various chemotherapeutic agents. Chk2, an ATP-dependent serine-threonine kinase, is a key component in the DNA replication-monitoring checkpoint system and is activated by double-stranded breaks (DSBs); activated chk2 is overexpressed by a variety of cancer cell types.

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	20.43	46.83
DMF	20.0	45.84
DMF:PBS (pH 7.2) (1:1)	0.5	1.15

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.29 mL	11.46 mL	22.92 mL
5 mM	0.46 mL	2.29 mL	4.58 mL
10 mM	0.23 mL	1.15 mL	2.29 mL
50 mM	0.05 mL	0.23 mL	0.46 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. van Harten AM, Buijze M, van der Mast R, Rooimans MA, Martens-de Kemp SR, Bachas C, Brink A, Stigter-van Walsum M, Wolthuis RMF, Brakenhoff RH. Targeting the cell cycle in head and neck cancer by Chk1 inhibition: a novel concept of bimodal cell death. Oncogenesis. 2019 Jun 17;8(7):38. doi: 10.1038/s41389-019-0147-x. PMID: 31209198; PMCID: PMC6572811.
2. Zhao J, Niu X, Li X, Edwards H, Wang G, Wang Y, Taub JW, Lin H, Ge Y. Inhibition of CHK1 enhances cell death induced by the Bcl-2-selective inhibitor ABT-199 in acute myeloid leukemia cells. Oncotarget. 2016 Jun 7;7(23):34785-99. doi: 10.18632/oncotarget.9185. PMID: 27166183; PMCID: PMC5085189.

In vivo study

1. King C, Diaz H, Barnard D, Barda D, Clawson D, Blosser W, Cox K, Guo S, Marshall M. Characterization and preclinical development of LY2603618: a selective and potent Chk1 inhibitor. Invest New Drugs. 2014 Apr;32(2):213-26. doi: 10.1007/s10637-013-0036-7. Epub 2013 Oct 10. PMID: 24114124.

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2. Barnard D, Diaz HB, Burke T, Donoho G, Beckmann R, Jones B, Barda D, King C, Marshall M. LY2603618, a selective CHK1 inhibitor, enhances the anti-tumor effect of gemcitabine in xenograft tumor models. Invest New Drugs. 2016 Feb;34(1):49-60. doi: 10.1007/s10637-015-0310-y. Epub 2015 Nov 27. PMID: 26612134.

7. Bioactivity

Biological target:

Rabusertib (LY2603618) is a potent and selective inhibitor of Chk1 with an IC50 of 7 nM.

In vitro activity

To further investigate cell death in a larger panel of cell lines and to exclude dose-dependent cell death, this study performed an ApoTox-Glo Triplex assay (Promega) with multiple concentrations of LY2603618/Rabusertib (Fig. 5a and S4c). Sensitive cell lines UM-SCC-22A and UM-SCC-38 both showed a rise in active caspase 3/7, a known marker for apoptosis execution, in relation to an increasing concentration of LY2603618/Rabusertib after 24 h, with a negligible increase of caspase-independent cytotoxicity (Fig. 5a).

Reference: Oncogenesis. 2019 Jul; 8(7): 38. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6572811/

In vivo activity

In order to assess the effects on DNA damage response resulting from combining LY2603618 with gemcitabine, mice implanted with Calu-6 tumor xenografts were administered vehicle, 150 mg/kg gemcitabine, 200 mg/kg LY2603618 or gemcitabine plus LY2603618 concurrently. Tumors were removed either 8 or 24 h later and analyzed by immunoblot for phosphorylation of CHK1 serine 345 by ATR, CHK1 serine 296 autophosphorylation and H2AX serine 139 phosphorylation (Fig. 4a, b, c). Although activated by gemcitabine at both 8 and 24 h, CHK1 activity is strongly inhibited by co-administration of LY2603618 for at least 24 h. As shown previously, LY2603618 did not inhibit the phosphorylation of CHK1 on serine 345 by ATR. CHK1 serine 345 phosphorylation increased after 8 h of combination treatment as described previously for other CHK1 inhibitors. In this xenograft model, treatment with gemcitabine alone caused minimal double-stranded DNA breaks as indicated by no increase in pH2AX (S139) levels. However when gemcitabine and LY2603618 are combined, a two-fold increase in pH2AX (S139) was measured in as little as 8 h and further increased nearly four-fold by 24 h, indicating an accumulation of DNA damage in the tumors.

Reference: Invest New Drugs. 2016 Feb;34(1):49-60. https://pubmed.ncbi.nlm.nih.gov/26612134/

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.