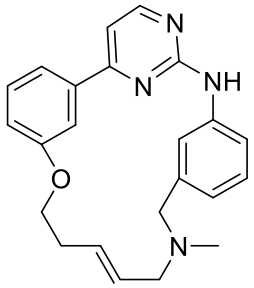
Product data sheet

MedKoo Cat#: 205642 Name: Zotiraciclib free base CAS#: 1204918-72-8 (free base) Chemical Formula: $C_{23}H_{24}N_4O$ Exact Mass: 372.19501 Molecular Weight: 372.46	
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:
Zotiraciclib, also known as TG02 and SB1317, is a novel small molecule potent CDK/JAK2/FLT3 inhibitor. Zotiraciclib may be useful for the treatment of cancer that crosses the blood brain barrier and acts by depleting Myc through the inhibition of cyclin-dependent kinase 9 (CDK9). It is one of a number of CDK inhibitors under investigation; others targeting CDK9 for the treatment of acute myeloid leukemia include alvocidib and atuveciclib. Myc overexpression is a known factor in many cancers, with 80 percent of glioblastomas characterized by this property.

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	26.5	71.15

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.68 mL	13.42 mL	26.85 mL
5 mM	0.54 mL	2.68 mL	5.37 mL
10 mM	0.27 mL	1.34 mL	2.68 mL
50 mM	0.05 mL	0.27 mL	0.54 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. Pasha MK, Jayaraman R, Reddy VP, Yeo P, Goh E, Williams A, Goh KC, Kantharaj E. Preclinical metabolism and pharmacokinetics of SB1317 (TG02), a potent CDK/JAK2/FLT3 inhibitor. Drug Metab Lett. 2012 Mar;6(1):33-42. doi: 10.2174/187231212800229336. PMID: 22372550.

In vivo study

1. William AD, Lee AC, Goh KC, Blanchard S, Poulsen A, Teo EL, Nagaraj H, Lee CP, Wang H, Williams M, Sun ET, Hu C, Jayaraman R, Pasha MK, Ethirajulu K, Wood JM, Dymock BW. Discovery of kinase spectrum selective macrocycle (16E)-14-methyl-20-oxa-5,7,14,26-tetraazatetracyclo[19.3.1.1(2,6).1(8,12)]heptacosa-1(25),2(26),3,5,8(27),9,11,16,21,23-decaene (SB1317/TG02), a potent inhibitor of cyclin dependent kinases (CDKs), Janus kinase 2 (JAK2), and fms-like tyrosine kinase-3 (FLT3) for the treatment of cancer. J Med Chem. 2012 Jan 12;55(1):169-96. doi: 10.1021/jm201112g. Epub 2011 Dec 29. PMID: 22148278.

7. Bioactivity
Biological target:

Product data sheet

Zotiraciclib (TG02; SB1317) is a potent inhibitor of CDK2, JAK2, and FLT3 for the treatment of cancer, with IC50s of 13, 73, and 56 nM for CDK2, JAK2 and FLT3, respectively.

In vitro activity

Zotiraciclib (SB1317) was soluble, highly permeable in Caco-2 cells, and showed > 99% binding to plasma from mice, dog and humans. It was metabolically stable in human and dog liver microsomes relative to mouse and rat. SB1317 was mainly metabolized by CYP3A4 and CY1A2 in vitro. SB1317 did not inhibit any of the major human CYPs in vitro except CYP2D6 (IC50=1 μM). SB1317 did not significantly induce CYP1A and CYP3A4 in human hepatocytes in vitro. The metabolic profiles in liver microsomes from preclinical species were qualitatively similar to humans.

Reference: Drug Metab Lett. 2012 Mar;6(1):33-42. http://www.eurekaselect.com/97785/article

In vivo activity

Two models were selected based on their relevance in cancer: HCT-116 colon cancer and Ramos B-cell lymphoma. Prior to conducting both experiments, dosing regimes in each model were explored and optimal schedules selected for each model that would be tolerated for the duration of the experiment. In the colon cancer model, HCT-116 cells were injected subcutaneously and tumors were established with mean group sizes of approximately 100 mm3. Treatment with Zotiraciclib (26h) at doses of 50 and 75 mg/kg po 3 times per week on a Monday, Wednesday, Friday schedule was started 8 days after cell inoculation for 15 days. Treatment with 26h at 75 mg/kg po q.d. 3×/week significantly inhibited the growth of tumors with a mean TGI of 82%, while the lower dose of 50 mg/kg po 3×/week was marginally effective (Figure 9). In the lymphoma model Ramos cells were injected subcutaneously and tumors were established with mean group sizes of approximately 200 mm3. Two different dosing regimens of 26h were explored in this model: 75 mg/kg po q.d. on a 2 days on and 5 days off schedule and 15 mg/kg ip q.d. on a 5 days on 5 days off schedule were started 12 days after cell inoculation for 15 days. There were two vehicle control groups that received either MC/Tween or DMA/CRE (see Experimental Section for details). The treatment groups were compared with the corresponding vehicle control groups for assessment of percentage TGI. Treatment with 26h using either regime significantly inhibited the growth of tumors with mean TGIs of 42% and 63% for the oral and ip delivery methods, respectively (Figure 10).

Reference: J Med Chem. 2012 Jan 12;55(1):169-96. https://doi.org/10.1021/jm201112g

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.