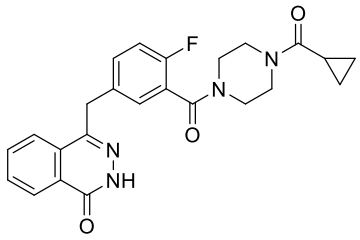
Product data sheet

MedKoo Cat#: 200422 Name: Olaparib (AZD-2281) CAS#: 763113-22-0 Chemical Formula: C24H23FN4O3 Exact Mass: 434.17542 Molecular Weight: 434.46	
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:
Olaparib, also known as AZD-2281 or KU-59436 , is a small molecule inhibitor of the nuclear enzyme poly(ADP-ribose) polymerase (PARP) with potential chemosensitizing, radiosensitizing, and antineoplastic activities. Olaparib selectively binds to and inhibits PARP, inhibiting PARP-mediated repair of single strand DNA breaks; PARP inhibition may enhance the cytotoxicity of DNA-damaging agents and may reverse tumor cell chemoresistance and radioresistance. PARP catalyzes post-translational ADP-ribosylation of nuclear proteins and can be activated by single-stranded DNA breaks. Olaparib was approved in 2014 for treating advanced ovarian cancer.

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	10.0	23.0

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.30 mL	11.51 mL	23.02 mL
5 mM	0.46 mL	2.30 mL	4.60 mL
10 mM	0.23 mL	1.15 mL	2.30 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. Ahmad A, Haas De Mello A, Szczesny B, Törö G, Marcatti M, Druzhyna N, Liaudet L, Tarantini S, Salomao R, Garcia Soriano F, Szabo C. Effects of the Poly(ADP-Ribose) Polymerase Inhibitor Olaparib in Cerulein-Induced Pancreatitis. Shock. 2020 May;53(5):653-665. doi: 10.1097/SHK.0000000000001402. PMID: 31274831; PMCID: PMC6944774.
2. Bianchi A, Lopez S, Altwerger G, Bellone S, Bonazzoli E, Zammataro L, Manzano A, Manara P, Perrone E, Zeybek B, Han C, Menderes G, Ratner E, Silasi DA, Huang GS, Azodi M, Newberg JY, Pavlick DC, Elvin J, Frampton GM, Schwartz PE, Santin AD. PARP-1 activity (PAR) determines the sensitivity of cervical cancer to olaparib. Gynecol Oncol. 2019 Oct;155(1):144-150. doi: 10.1016/j.ygyno.2019.08.010. Epub 2019 Aug 18. PMID: 31434613; PMCID: PMC6788971.

In vivo study

1. Gu Z, Wang L, Yao X, Long Q, Lee K, Li J, Yue D, Yang S, Liu Y, Li N, Li Y. ClC-3/SGK1 regulatory axis enhances the olaparib-induced antitumor effect in human stomach adenocarcinoma. Cell Death Dis. 2020 Oct 22;11(10):898. doi: 10.1038/s41419-020-03107-3. PMID: 33093458; PMCID: PMC7583252.

2. Ahmad A, Vieira JC, de Mello AH, de Lima TM, Ariga SK, Barbeiro DF, Barbeiro HV, Szczesny B, Törö G, Druzhyna N, Randi EB, Marcatti M, Toliver-Kinsky T, Kiss A, Liaudet L, Salomao R, Soriano FG, Szabo C. The PARP inhibitor olaparib exerts beneficial effects in mice subjected to cecal ligature and puncture and in cells subjected to oxidative stress without impairing DNA integrity: A potential opportunity for repurposing a clinically used oncological drug for the experimental therapy of sepsis. Pharmacol Res. 2019 Jul;145:104263. doi: 10.1016/j.phrs.2019.104263. Epub 2019 May 6. PMID: 31071432; PMCID: PMC6662650.

7. Bioactivity

Biological target:

Olaparib (AZD2281; KU0059436) is a PARP inhibitor with IC50s of 5 and 1 nM for PARP1 and PARP2, respectively.

In vitro activity

In HPDE cells subjected to oxidative stress, olaparib inhibited PARylation (as measured by the quantification of poly(ADP-ribose) [PAR], the product of the enzyme) already at the lowest concentration (1 μM) used, confirming the well-established potent inhibitory effect of olaparib on PARP1 catalytic activity in this cell line (Fig. 8). PARP1 enzyme levels were downregulated by the oxidative stress challenge; this downregulation was also partially attenuated by the lower concentrations (1–3 μM) of olaparib (Fig. 8). In line with prior findings demonstrating that PARP inhibition prevents the cellular depletion of its substrate, NAD^+, olaparib also protected against the H_2O_2-induced loss of cellular NAD^+ levels, with the effects already near-maximal at its lowest concentration tested (1 μM) (Fig. 9).

Reference: Shock. 2020 May; 53(5): 653–665. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6944774/

In vivo activity

In young adult male mice subjected to CLP, olaparib (1, 3 or 10 mg/kg i.p.) concentration-dependently improved several parameters of multiorgan dysfunction (Figs. 1–3). For instance, the CLP-induced increases in spleen MPO content and liver and spleen MDA levels were attenuated by olaparib (Fig. 1). In addition, the CLP-induced increases in plasma markers of liver and pancreas injury (ALP, ALT, amylase) and renal dysfunction (BUN) were attenuated by olaparib treatment (Fig. 2). The histopathological pictures of the lungs did not show marked alterations in any of the groups, with slight emphysema evident in all CLP groups (Fig. 3). In the liver, foamy degeneration of numerous hepatocytes is evident in the CLP group; olaparib, at the 10 mg/kg dose, normalized the morphology of the hepatocytes (Fig. 4). In the spleen, CLP induced macrophage infiltration, and evidence of hemolysis was evident, with no marked differences between CLP groups with or without olaparib (Fig. 5).

Reference: Pharmacol Res. 2019 Jul; 145: 104263. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6662650/