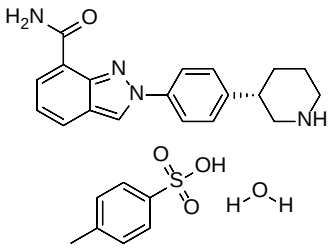
Product data sheet

MedKoo Cat#: 330234 Name: Niraparib tosylate hydrate CAS: 1613220-15-7 (tosylate hydrate) Chemical Formula: $C_{26}H_{30}N_4O_5S$ Molecular Weight: 510.609	
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:
Niraparib, also know as MK-4827, is an inhibitor of poly (ADP-ribose) polymerase (PARP) with potential antineoplastic activity. MK4827 inhibits PARP activity, enhancing the accumulation of DNA strand breaks and promoting genomic instability and apoptosis. The PARP family of proteins detect and repair single strand DNA breaks by the base-excision repair (BER) pathway.

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
TBD	TBD	TBD

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	1.96 mL	9.79 mL	19.58 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. Sambade MJ, Van Swearingen AED, McClure MB, Deal AM, Santos C, Sun K, Wang J, Mikule K, Anders CK. Efficacy and pharmacodynamics of niraparib in BRCA-mutant and wild-type intracranial triple-negative breast cancer murine models. Neurooncol Adv. 2019 Jun 4;1(1):vdz005. doi: 10.1093/noajnl/vdz005. PMID: 32642648; PMCID: PMC7212882.

2. Li H, Tu J, Zhao Z, Chen L, Qu Y, Li H, Yao H, Wang X, Lee DF, Shen J, Wen L, Huang G, Xie X. Molecular signatures of BRCAness analysis identifies PARP inhibitor Niraparib as a novel targeted therapeutic strategy for soft tissue Sarcomas. Theranostics. 2020 Jul 25;10(21):9477-9494. doi: 10.7150/thno.45763. PMID: 32863940; PMCID: PMC7449912. (synergistic)

In vivo study

1. Sun K, Mikule K, Wang Z, Poon G, Vaidyanathan A, Smith G, Zhang ZY, Hanke J, Ramaswamy S, Wang J. A comparative pharmacokinetic study of PARP inhibitors demonstrates favorable properties for niraparib efficacy in preclinical tumor models. Oncotarget. 2018 Dec 14;9(98):37080-37096. doi: 10.18632/oncotarget.26354. PMID: 30647846; PMCID: PMC6324689.

2. AlHilli MM, Becker MA, Weroha SJ, Flatten KS, Hurley RM, Harrell MI, Oberg AL, Maurer MJ, Hawthorne KM, Hou X, Harrington SC, McKinstry S, Meng XW, Wilcoxen KM, Kalli KR, Swisher EM, Kaufmann SH, Haluska P. In vivo anti-tumor activity of the PARP inhibitor niraparib in homologous recombination deficient and proficient ovarian carcinoma. Gynecol Oncol. 2016 Nov;143(2):379-388. doi: 10.1016/j.ygyno.2016.08.328. Epub 2016 Sep 8. PMID: 27614696; PMCID: PMC5370566.

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7. Bioactivity

Biological target:

Niraparib (MK-4827) tosylate hydrate is a highly potent and orally bioavailable PARP1 and PARP2 inhibitor with IC_{50}s of 3.8 and 2.1 nM.

In vitro activity

This study aimed to explore the genomic and molecular landscape of BRCAness using whole exome sequencing (WES) in STS, aiming to find a potential target for STS treatment. To reveal the possible genomic and molecular characteristics of STS, analyses were performed in 22 STS tumor samples from the First Affiliated Hospital of Sun Yat-sen University by comparing with their matched normal adjacent tissues using WES. DNA damage was induced by a topoisomerase II inhibitor (etoposide) and PARPi niraparib (MK4827) in normal fibroblasts and STS cell lines (HT-1080, RD, SW982, VA-ES-BJ, SK-LMS-1, SW872). We subsequently investigated the potency of niraparib (MK4827) in STS in vitro using MTT assays (Figure S3A). The MTT assay results showed that STS cell lines were sensitive to MK4827. Moreover, with the downregulation of PARP-1 expression, fibroblasts were less sensitive to MK4827 than STS cell lines. Among the five FDA-approved PARPis, niraparib was a more potent and less cytotoxic PARPi for STS treatment. Moreover, according to the screening combination test for cytotoxic regimens therapy for STS (doxorubicin, ifosfamide, dacarbazine, and TMZ), we found that niraparib and TMZ were the most synergistically effective among all STS cell line combination therapies. Our finding provided a novel potential targeted therapeutic strategy for patients with STS.

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https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7449912/

In vivo activity

To explore whether the biophysical properties intrinsic to niraparib, such as high permeability and VD, may contribute to its broader clinical activity in patients with or without BRCA mutations, the pharmacokinetic profiles and efficacies of niraparib and olaparib were compared in preclinical tumor models. Niraparib was administered at 25, 50, or 75 mg/kg once daily for 28 days to mice bearing MDA-MB-436 BRCAmut tumors. Suppression of tumor growth was observed at all doses with TGIs of 60%, 93%, and 107%, respectively The tissue distribution of niraparib and olaparib were also compared in both the MDA-MB-436 and OVC134 models. After 5-day treatment in the MDA-MB-436 model or 2-day treatment in the OVC134 model, niraparib tumor exposure was 3.3-fold of plasma exposure (Figure 2A & 2C and Table 3), suggesting that niraparib tends to concentrate in tumor relative to plasma. Niraparib demonstrated greater efficacy compared to olaparib in vivo, a phenotype that could, at least partially, be attributed to their different pharmacokinetic properties, i.e. VD and cell permeability. This may also explain why niraparib has shown stronger activity in non-BRCAmut patients in clinical studies. Our results show that niraparib tumor exposure is significantly higher than plasma exposure, which is consistent with its high VD. In comparison, olaparib tumor exposure is lower than plasma exposure. In addition, niraparib permeates the brain, whereas olaparib shows very limited brain exposure at maximum tolerated dose (MTD). Importantly, in BRCAwt tumor xenograft models and an intracranial tumor model, niraparib achieved more potent tumor growth inhibition than olaparib.

Oncotarget. 2018 Dec 14; 9(98): 37080–37096.Published online 2018 Dec 14.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6324689/

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.