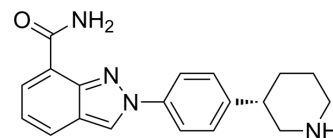


Niraparib

Cat. No.:	HY-10619		
CAS No.:	1038915-60-4		
Molecular Formula:	C ₁₉ H ₂₀ N ₄ O		
Molecular Weight:	320.39		
Target:	PARP; Apoptosis		
Pathway:	Cell Cycle/DNA Damage; Epigenetics; Apoptosis		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	1 year
		-20°C	6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : 31.25 mg/mL (97.54 mM); ultrasonic and warming and heat to 60°C
 H₂O : < 0.1 mg/mL (ultrasonic;warming;heat to 80°C) (insoluble)

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	3.1212 mL	15.6060 mL	31.2120 mL
	5 mM	0.6242 mL	3.1212 mL	6.2424 mL
	10 mM	0.3121 mL	1.5606 mL	3.1212 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

- Add each solvent one by one: 50% PEG300 >> 50% saline
Solubility: 2.5 mg/mL (7.80 mM); Clear solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 2.08 mg/mL (6.49 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 2.08 mg/mL (6.49 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.08 mg/mL (6.49 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Niraparib (MK-4827) is a highly potent and orally bioavailable PARP1 and PARP2 inhibitor with IC₅₀s of 3.8 and 2.1 nM, respectively. Niraparib leads to inhibition of repair of DNA damage, activates apoptosis and shows anti-tumor activity^{[1][2][3]}.

IC₅₀ & Target

PARP-2	PARP-1	V-PARP	TANK-1
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	2.1 nM (IC ₅₀)	3.8 nM (IC ₅₀)	330 nM (IC ₅₀)	570 nM (IC ₅₀)								
	PARP-3 1300 nM (IC ₅₀)											
In Vitro	<p>Niraparib (MK-4827) inhibits PARP activity with EC₅₀=4 nM and EC₉₀=45 nM in a whole cell assay. MK-4827 inhibits proliferation of cancer cells with mutant BRCA-1 and BRCA-2 with CC₅₀ in the 10-100 nM range. MK-4827 displays excellent PARP 1 and 2 inhibition with IC₅₀=3.8 and 2.1 nM, respectively, and in a whole cell assay^[1]. To validate that Niraparib (MK-4827) inhibits PARP in these cell lines, A549 and H1299 cells are treated with 1 μM MK-4827 for various times and measured PARP enzymatic activity using a chemiluminescent assay. The results show that Niraparib (MK-4827) inhibits PARP within 15 minutes of treatment reaching about 85% inhibition in the A549 cells at 1 h and about 55% inhibition at 1 h for the H1299 cells^[2].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>											
In Vivo	<p>Niraparib (MK-4827) is well tolerated and demonstrates efficacy as a single agent in a xenograft model of BRCA-1 deficient cancer. Niraparib (MK-4827) is well tolerated in vivo and demonstrates efficacy as a single agent in a xenograft model of BRCA-1 deficient cancer. Niraparib (MK-4827) is characterized by acceptable pharmacokinetics in rats with plasma clearance of 28 (mL/min)/kg, very high volume of distribution (Vd_{ss}=6.9 L/kg), long terminal half-life (t_{1/2}=3.4 h), and excellent bioavailability, F=65%^[1]. Niraparib (MK-4827) enhances radiation response of p53 mutant Calu-6 tumor in both cases, with the single daily dose of 50 mg/kg being more effective than 25 mg/kg given twice daily^[3].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> <table border="1"> <tbody> <tr> <td>Animal Model:</td> <td>Female nude mice (Ncr Nu/Nu) with solitary tumor xenografts^[3]</td> </tr> <tr> <td>Dosage:</td> <td>25 mg/kg or 50 mg/kg</td> </tr> <tr> <td>Administration:</td> <td>Gavage, 25 mg/kg twice a day with 6 h between doses or 50 mg/kg once daily for 21 consecutive days</td> </tr> <tr> <td>Result:</td> <td>Enhanced radiation response.</td> </tr> </tbody> </table>				Animal Model:	Female nude mice (Ncr Nu/Nu) with solitary tumor xenografts ^[3]	Dosage:	25 mg/kg or 50 mg/kg	Administration:	Gavage, 25 mg/kg twice a day with 6 h between doses or 50 mg/kg once daily for 21 consecutive days	Result:	Enhanced radiation response.
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Result:	Enhanced radiation response.											

CUSTOMER VALIDATION

- Cancer Cell. 2020 Dec 14;38(6):844-856.e7.
- Cancer Discov. 2017 Sep;7(9):984-998.
- Cancer Discov. 2017 Sep;7(9):984-998.
- Nat Biomed Eng. 2023 Jul 24.
- Nat Commun. 2022 Nov 19;13(1):7107.

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REFERENCES

[1]. Jones P, et al. Discovery of 2-[4-[(3S)-piperidin-3-yl]phenyl]-2H-indazole-7-carboxamide (MK-4827): a novel oral poly(ADP-ribose)polymerase (PARP) inhibitor efficacious in BRCA-1 and -2 mutant tumors. *J Med Chem*. 2009 Nov 26;52(22):7170-85.

[2]. Bridges KA, et al. Niraparib (MK-4827), a novel poly(ADP-Ribose) polymerase inhibitor, radiosensitizes human lung and breast cancer cells. *Oncotarget*. 2014 Jul 15;5(13):5076-86.

[3]. Wang L, et al. MK-4827, a PARP-1/-2 inhibitor, strongly enhances response of human lung and breast cancer xenografts to radiation. *Invest New Drugs*. 2012 Dec;30(6):2113-20.

Caution: Product has not been fully validated for medical applications. For research use only.

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