Niraparib tosylate hydrate

Cat. No.: HY-10619E

CAS No.: 1613220-15-7

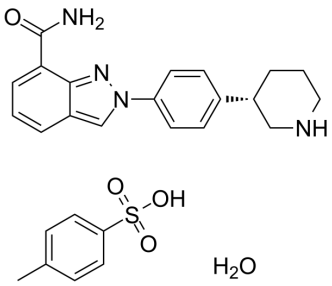
Molecular Formula: $C_{26}H_{30}N_4O_5S$

Molecular Weight: 510.61

Target: PARP; Apoptosis

Pathway: Cell Cycle/DNA Damage; Epigenetics; Apoptosis

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (97.92 mM; Need ultrasonic)

Preparing Stock Solutions	Concentration / Solvent / Mass	1 mg	5 mg	10 mg
	1 mM	1.9584 mL	9.7922 mL	19.5844 mL
	5 mM	0.3917 mL	1.9584 mL	3.9169 mL
	10 mM	0.1958 mL	0.9792 mL	1.9584 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.90 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.90 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.90 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

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, respectively. Niraparib tosylate hydrate leads to inhibition of repair of DNA damage, activates apoptosis and shows anti-tumor activity[1][2][3].

IC_{50} & Target

PARP-2	PARP-1	V-PARP	TANK-1
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	Niraparib (MK-4827) tosylate hydrate inhibits PARP activity with EC_{50}=4 nM and EC_{90}=45 nM in a whole cell assay. Niraparib tosylate hydrate inhibits proliferation of cancer cells with mutant BRCA-1 and BRCA-2 with CC_{50} in the 10-100 nM range. Niraparib tosylate hydrate displays excellent PARP 1 and 2 inhibition with IC_{50}=3.8 and 2.1 nM, respectively, and in a whole cell assay[1]. Niraparib tosylate hydrate 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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Niraparib (MK-4827) tosylate hydrate is well tolerated and demonstrates efficacy as a single agent in a xenograft model of BRCA-1 deficient cancer[1]. Niraparib (MK-4827) tosylate hydrate is well tolerated in vivo and demonstrates efficacy as a single agent in a xenograft model of BRCA-1 deficient cancer[1]. Niraparib (MK-4827) tosylate hydrate 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) tosylate hydrate 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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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.

CUSTOMER VALIDATION

- Cancer Cell. 2020 Dec 14;38(6):844-856.e7.
- Cancer Discov. 2017 Sep;7(9):984-998.
- Nat Biomed Eng. 2023 Jul 24.
- Nat Commun. 2022 Nov 19;13(1):7107.
- J Clin Invest. 2019 Mar 1;129(3):1211-1228.

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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.

[4]. Mirza MR, et al. Niraparib Maintenance Therapy in Platinum-Sensitive, Recurrent Ovarian Cancer. N Engl J Med. 2016 Dec 1;375(22):2154-2164.

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

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