Niraparib tosylate hydrate

Cat. No.: HY-10619E

CAS No.: 1613220-15-7

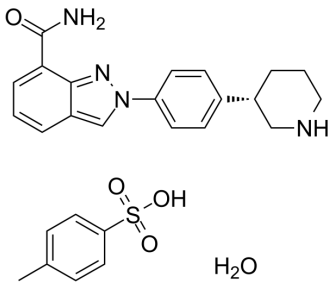
Molecular Formula: $C_{26}H_{30}N_4O_5S$

Molecular Weight: 510.61

Target: PARP; Apoptosis

Pathway: Cell Cycle/DNA Damage; Epigenetics; Apoptosis

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



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].

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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 Discov. 2017 Sep;7(9):984-998.
- Cancer Cell. 2020 Dec 14;38(6):844-856.e7.
- J Clin Invest. 2019 Mar 1;129(3):1211-1228.
- Clin Cancer Res. 2017 Feb 15;23(4):1001-1011.
- Cancer Res. 2022 Apr 26:canres.CAN-22-0742-E.2022.

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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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