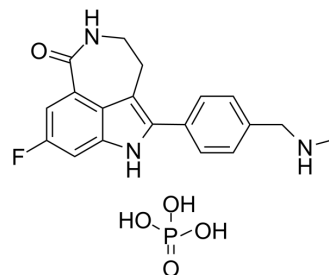


Rucaparib phosphate

Cat. No.:	HY-10617
CAS No.:	459868-92-9
Molecular Formula:	C ₁₉ H ₂₁ FN ₃ O ₅ P
Molecular Weight:	421.36
Target:	PARP
Pathway:	Cell Cycle/DNA Damage; Epigenetics
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 : ≥ 33 mg/mL (78.32 mM)
 H₂O : 5 mg/mL (11.87 mM); ultrasonic and warming and heat to 60°C
 * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	2.3733 mL	11.8663 mL	23.7327 mL
	5 mM	0.4747 mL	2.3733 mL	4.7465 mL
	10 mM	0.2373 mL	1.1866 mL	2.3733 mL

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

In Vivo

- Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
Solubility: ≥ 2.5 mg/mL (5.93 mM); Clear solution
- Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
Solubility: ≥ 2.5 mg/mL (5.93 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 2.17 mg/mL (5.15 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 2.17 mg/mL (5.15 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.17 mg/mL (5.15 mM); Clear solution
- Add each solvent one by one: 1% DMSO >> 99% saline
Solubility: ≥ 0.5 mg/mL (1.19 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	Rucaparib (AG014699) phosphate is an orally active, potent inhibitor of PARP proteins (PARP-1, PARP-2 and PARP-3) with a K_i of 1.4 nM for PARP1. Rucaparib phosphate is a modest hexose-6-phosphate dehydrogenase (H6PD) inhibitor. Rucaparib phosphate has the potential for castration-resistant prostate cancer (CRPC) research ^{[1][2][3][4]} .																						
IC₅₀ & Target	PARP-1 1.4 nM (K _i)	PARP-2	PARP-3																				
In Vitro	<p>Rucaparib (AG014699) phosphate is a possible N-demethylation metabolite of AG14644^[1].</p> <p>Rucaparib (0.1, 1, 10, 100 μM; 24 hours) phosphate is cytotoxic and has the LC₅₀ being 5 μM in Capan-1 (BRCA2 mutant) cells and only 100 nM in MX-1 (BRCA1 mutant) cells^[2].</p> <p>The radio-sensitization by Rucaparib phosphate is due to downstream inhibition of activation of NF-κB, and is independent of SSB repair inhibition. Rucaparib phosphate can target NF-κB activated by DNA damage and overcome toxicity observed with classical NF-κB inhibitors without compromising other vital inflammatory functions^[5].</p> <p>Rucaparib phosphate inhibits PARP-1 activity by 97.1% at a concentration of 1 μM in permeabilised D283Med cells^[6]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>																						
In Vivo	<p>Rucaparib (AG014699) phosphate and AG14584 significantly increase Temozolomide toxicity. Rucaparib (1 mg/kg) phosphate significantly increases Temozolomide-induced body weight loss. Rucaparib (0.1 mg/kg) phosphate results in a 50% increase in the temozolomide-induced tumor growth delay^[1].</p> <p>Rucaparib (10 mg/kg for i.p. or 50, 150 mg/kg for p.o.; daily for 5 days per week for 6 weeks) phosphate significantly inhibits the growth of the tumor, and there is one complete tumor regression and two persistent partial regressions^[2].</p> <p>Rucaparib (150 mg/kg; p.o.; once per week for 6 weeks or three times per week for 6 weeks) phosphate has greatest antitumor effect with three complete regressions^[2].</p> <p>Rucaparib phosphate enhances the antitumor activity of temozolomide and indicates complete and sustained tumor regression in NB1691 and SHSY5Y xenografts^[6].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 30%;">Animal Model:</td> <td>Female athymic nude mice, implanted SW620 colorectal tumor cells (1×10^7 cells per animal) s.c.^[1]</td> </tr> <tr> <td>Dosage:</td> <td>0.1 mg/kg in combination with Temozolomide (p.o., 200 mg/kg), 0.05, 0.15, and 0.5 mg/kg in combination with Temozolomide (p.o., 68 mg/kg) or 10 mg/kg</td> </tr> <tr> <td>Administration:</td> <td>IP, single dose for 0.1 mg/kg and 10 mg/kg, five daily doses for 0-0.5 mg/kg</td> </tr> <tr> <td>Result:</td> <td>Significantly increased Temozolomide toxicity, showed outstanding chemosensitization potency and caused enhancement of Temozolomide-induced tumor growth delay</td> </tr> </table> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 30%;">Animal Model:</td> <td>CD-1 nude mice bearing established Capan-1 xenografts^[2]</td> </tr> <tr> <td>Dosage:</td> <td>10 mg/kg or 50, 100 and 150 mg/kg</td> </tr> <tr> <td>Administration:</td> <td>IP for 10 mg/kg; PO for 50, 100 and 150 mg/kg, single dose (Pharmacokinetics)</td> </tr> <tr> <td>Result:</td> <td>Parent drug was detectable in the plasma only at 30 min after 10 mg/kg i.p and up to 4 h for 50–150 mg/kg p.o.. Was still detectable in most mice receiving oral rucaparib at 3 days. Does not easily cross the plasma membrane.</td> </tr> </table> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 30%;">Animal Model:</td> <td>CD-1 nude mice bearing established Capan-1 xenografts^[2]</td> </tr> <tr> <td>Dosage:</td> <td>10 mg/kg i.p. daily for 5 days per week for 6 weeks, 50 or 150 mg/kg p.o. daily × five weekly × six, 150 mg/kg p.o. once per week for 6 weeks or three times per week for 6</td> </tr> </table>			Animal Model:	Female athymic nude mice, implanted SW620 colorectal tumor cells (1×10^7 cells per animal) s.c. ^[1]	Dosage:	0.1 mg/kg in combination with Temozolomide (p.o., 200 mg/kg), 0.05, 0.15, and 0.5 mg/kg in combination with Temozolomide (p.o., 68 mg/kg) or 10 mg/kg	Administration:	IP, single dose for 0.1 mg/kg and 10 mg/kg, five daily doses for 0-0.5 mg/kg	Result:	Significantly increased Temozolomide toxicity, showed outstanding chemosensitization potency and caused enhancement of Temozolomide-induced tumor growth delay	Animal Model:	CD-1 nude mice bearing established Capan-1 xenografts ^[2]	Dosage:	10 mg/kg or 50, 100 and 150 mg/kg	Administration:	IP for 10 mg/kg; PO for 50, 100 and 150 mg/kg, single dose (Pharmacokinetics)	Result:	Parent drug was detectable in the plasma only at 30 min after 10 mg/kg i.p and up to 4 h for 50–150 mg/kg p.o.. Was still detectable in most mice receiving oral rucaparib at 3 days. Does not easily cross the plasma membrane.	Animal Model:	CD-1 nude mice bearing established Capan-1 xenografts ^[2]	Dosage:	10 mg/kg i.p. daily for 5 days per week for 6 weeks, 50 or 150 mg/kg p.o. daily × five weekly × six, 150 mg/kg p.o. once per week for 6 weeks or three times per week for 6
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	weeks, or 150 mg/kg p.o. daily for five days every 3 weeks
Administration:	IP or PO
Result:	10 mg/kg i.p. significantly inhibited the growth of the tumor, daily oral administration at 150 mg/kg had an equivalent effect on tumor growth to 10 mg/kg i.p.. The schedule with the greatest antitumor effect was oral administration of 150 mg/kg on a once weekly schedule with three complete regressions.
Animal Model:	CD-1 nude mice, NB1691 and SHSY5Y xenografts ^[6]
Dosage:	1 mg/kg
Administration:	IP, daily for 5 d in combination with Temozolomide (orally daily ×5 at a dose of 68 mg/kg)
Result:	Enhanced the antitumor activity of Temozolomide and indicated complete and sustained tumor regression.

CUSTOMER VALIDATION

- Nat Methods. 2023 Jul 20.
- Sci Transl Med. 2021 May 26;13(595):eabe8226.
- Sci Adv. 2022 Feb 18;8(7):eabl9794.
- Theranostics. 2020 Jul 25;10(21):9477-9494.
- Clin Cancer Res. 2017 Feb 15;23(4):1001-1011.

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REFERENCES

- [1]. Thomas HD, et al. Preclinical selection of a novel poly(ADP-ribose) polymerase inhibitor for clinical trial. Mol Cancer Ther, 2007, 6(3), 945-956.
- [2]. Hunter JE, et al. NF-κB mediates radio-sensitization by the PARP-1 inhibitor, AG-014699. Oncogene, 2012, 31(2), 251-264.
- [3]. Daniel RA, et al. Inhibition of poly(ADP-ribose) polymerase-1 enhances temozolomide and topotecan activity against childhood neuroblastoma. Clin Cancer Res, 2009, 15(4), 1241-1249.
- [4]. Matt Shirley, et al. Rucaparib: A Review in Ovarian Cancer. Target Oncol. 2019 Apr;14(2):237-246.
- [5]. Jianneng Li, et al. Hexose-6-phosphate dehydrogenase blockade reverses prostate cancer drug resistance in xenograft models by glucocorticoid inactivation. Sci Transl Med. 2021 May 26;13(595):eabe8226.
- [6]. J Murray, et al. Tumour cell retention of rucaparib, sustained PARP inhibition and efficacy of weekly as well as daily schedules. Br J Cancer. 2014 Apr 15;110(8):1977-84.

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Tel: 609-228-6898

Fax: 609-228-5909

E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA