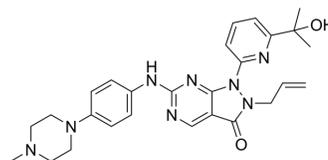


## Adavosertib

Cat. No.:	HY-10993		
CAS No.:	955365-80-7		
Molecular Formula:	C <sub>27</sub> H <sub>32</sub> N <sub>8</sub> O <sub>2</sub>		
Molecular Weight:	500.6		
Target:	Wee1		
Pathway:	Cell Cycle/DNA Damage		
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 : 125 mg/mL (249.70 mM; Need ultrasonic)

Concentration	Mass		
	1 mg	5 mg	10 mg
1 mM	1.9976 mL	9.9880 mL	19.9760 mL
5 mM	0.3995 mL	1.9976 mL	3.9952 mL
10 mM	0.1998 mL	0.9988 mL	1.9976 mL

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

#### In Vivo

- Add each solvent one by one: 0.5% Methylcellulose/saline water  
Solubility: 5 mg/mL (9.99 mM); Suspension solution; Need ultrasonic
- Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline  
Solubility: ≥ 2.87 mg/mL (5.73 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
Solubility: ≥ 2.08 mg/mL (4.16 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
Solubility: ≥ 2.08 mg/mL (4.16 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil  
Solubility: ≥ 2.08 mg/mL (4.16 mM); Clear solution

### BIOLOGICAL ACTIVITY

#### Description

Adavosertib (AZD-1775; MK-1775) is a potent Wee1 inhibitor with an IC<sub>50</sub> of 5.2 nM.

#### IC<sub>50</sub> & Target

IC<sub>50</sub>: 5.2 nM (Wee1)

<b>In Vitro</b>	<p>Adavosertib (MK-1775) enhances the cytotoxic effects of 5-FU in p53-deficient human colon cancer cells. Adavosertib (MK-1775) inhibits CDC2 Y15 phosphorylation in cells, abrogates DNA damaged checkpoints induced by 5-FU treatment, and causes premature entry of mitosis determined by induction of Histone H3 phosphorylation<sup>[1]</sup>.</p> <p>Adavosertib (MK-1775) abrogates the radiation-induced G2 block in p53-defective cells but not in p53 wild-type lines<sup>[2]</sup>. The combination of NSC 613327 with Adavosertib (MK-1775) produces robust anti-tumor activity and remarkably enhances tumor regression response (4.01 fold) compared to NSC 613327 treatment in p53-deficient tumors<sup>[3]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
<b>In Vivo</b>	<p>In vivo, Adavosertib (MK-1775) potentiates the anti-tumor efficacy of 5-FU at tolerable doses<sup>[1]</sup>.</p> <p>Adavosertib (MK-1775) (60 mg/kg twice daily, p.o.) enhances H1299 xenograft tumor response to fractionated radiotherapy<sup>[2]</sup>.</p> <p>Adavosertib (MK-1775) (30 mg/kg, p.o.) regresses tumor growth in PANC198, PANC215 and PANC185 as compared to GEM treated mice<sup>[3]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

## PROTOCOL

<b>Cell Assay</b> <sup>[2]</sup>	<p>Total protein is extracted from the cell pellet using a lysis solution containing 50 mM HEPES (pH 7.9), 0.4 mol/L NaCl, and 1 mM EDTA and fortified with 10 µL/mL phosphatase inhibitor cocktail 1, 10 µL/mL phosphatase inhibitor cocktail 2, 10 µL/mL protease inhibitor, and 1% NP-40. Protein concentration of the lysates is determined by the Bio-Rad protein assay. Equal amounts of protein are separated by 12% SDS-PAGE and transferred to an Immobilon membrane. Nonspecific binding sites on the membrane are blocked in 5% nonfat dry milk in Tris (20 mM)-buffered saline (150 mM, pH 7.4) with 0.1% Tween (TBS-T). Protein signals are detected by incubating the membrane in primary antibody in 5% nonfat dry milk overnight at 4°C, followed by a 45-min incubation in the appropriate peroxidase-conjugated secondary antibody. The membrane is then developed by enhanced chemiluminescence with ECL plus Western Blotting Detection Reagents on a Typhoon 9400 scanner.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
<b>Animal Administration</b> <sup>[2]</sup>	<p>Tumor xenografts are produced in the leg by im inoculation of 1×10<sup>6</sup> Calu-6 cells in 10 µL. Irradiation and Adavosertib (MK-1775) treatment are started when tumors reach 8 mm diameter and continue for 5 days. Gamma-rays are delivered locally to the tumor-bearing legs of unanesthetized mice using a small-animal irradiator consisting of two parallel-opposed <sup>137</sup>Cs sources, at a dose rate of 5 Gy/min. Tumors are irradiated twice daily separated by 6 h. Adavosertib (MK-1775) is given by gavage in 0.1 mL volumes 1 h before and 2 h after the first daily radiation dose.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

## CUSTOMER VALIDATION

- Cancer Cell. 2022 Dec 20;S1535-6108(22)00565-7.
- J Hematol Oncol. 2018 Aug 1;11(1):99.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Sci Adv. 2021 Apr 30;7(18):eabd4676.
- Blood Cancer J. 2021 Jul 31;11(7):137.

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## REFERENCES

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[1]. Hirai H, et al. MK-1775, a small molecule Wee1 inhibitor, enhances anti-tumor efficacy of various DNA-damaging agents, including 5-FU. *Cancer Biol Ther.* 2010 Apr;9(7):514-22.

[2]. Bridges KA, et al. MK-1775, a novel Wee1 kinase inhibitor, radiosensitizes p53-defective human tumor cells. *Clin Cancer Res.* 2011 Sep 1;17(17):5638-48. Epub 2011 Jul 28.

[3]. Rajeshkumar NV, et al. MK-1775, a potent Wee1 inhibitor, synergizes with NSC 613327 to achieve tumor regressions, selectively in p53-deficient pancreatic cancer xenografts. *Clin Cancer Res.* 2011 May 1;17(9):2799-806. Epub 2011 Mar 9.

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

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