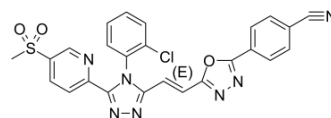


G007-LK

Cat. No.:	HY-12438		
CAS No.:	1380672-07-0		
Molecular Formula:	C ₂₅ H ₁₆ ClN ₇ O ₃ S		
Molecular Weight:	529.96		
Target:	PARP		
Pathway:	Cell Cycle/DNA Damage; Epigenetics		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 30 mg/mL (56.61 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent	Mass	1 mg	5 mg	10 mg
	Concentration				
	1 mM		1.8869 mL	9.4347 mL	18.8693 mL
	5 mM		0.3774 mL	1.8869 mL	3.7739 mL
	10 mM		0.1887 mL	0.9435 mL	1.8869 mL

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

BIOLOGICAL ACTIVITY

Description	G007-LK is a potent and selective inhibitor of TNKS1 and TNKS2, with IC ₅₀ s of 46 nM and 25 nM, respectively.	
IC ₅₀ & Target	TNKS2 25 nM (IC ₅₀)	TNKS1 46 nM (IC ₅₀)
In Vitro	G007-LK is a potent inhibitor of TNKS1 and TNKS2, with IC ₅₀ s of 46 nM and 25 nM, respectively, and a cellular IC ₅₀ of 50 nM. G007-LK shows no inhibition of PARP1 at doses up to 20 μM, and has a high CYP3A4 inhibition IC ₅₀ value (>25 μM) ^[1] . G007-LK (0-20 μM) dose-dependently inhibits hepatocellular carcinoma (HCC) cell growth. G007-LK also downregulates the levels of YAP by upregulating AMOTL1 and AMOTL2 in HCC cell lines. In addition, G007-LK (0-20 μM) synergizes with MEK and AKT inhibitors to suppress HCC cell proliferation ^[3] .	
In Vivo	G007-LK displays great pharmacokinetic profile in ICR mice ^[1] . G007-LK (100 mg/kg chow, p.o.) significantly reduces lineage tracing from LGR5 ⁺ intestinal stem cells in mice. G007-LK (100 mg/kg chow, p.o.) specifically targets LGR5 ⁺	

WNT-dependent intestinal stem cells in Lgr5-EGFP-CreERT2;R26R-tdTomato mice. G007-LK (10, 50 mg/kg, p.o.) also suppresses canonical WNT signalling. Furthermore, G007-LK (100, 1000 mg/kg chow, p.o) shows no effect on the alteration of duodenal morphology^[2].

PROTOCOL

Cell Assay ^[3]

For cell proliferation or apoptosis assays, **SNU-449** and **HLE** cells are grown in a 5% CO₂ atmosphere, at 37°C, in **RPMI Medium supplemented with 10% fetal bovine serum (FBS) and penicillin/streptomycin**. HCC cells are treated with 0.1% DMSO, or 2.5 μM, 5 μM, 10 μM, 20 μM **XAV-939** or **G007-LK**, either alone or in combination with the MEK inhibitor U0126 (25 μM) or the AKT inhibitor MK-2206 (5 μM). Cell proliferation is analyzed using the BrdU Cell Proliferation Assay Kit, while apoptosis is assessed with the Cell Death Detection Elisa Plus Kit^[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration ^[2]

Drug treatment experiments are performed with **wild type (wt)**, single or double **transgenic Lgr5-EGFP-Ires-CreERT2;R26R-Confetti** mice, unless indicated otherwise. **G007-LK is administered orally either by gavage (10 or 50 mg/kg body mass once daily, vehicle: 15% dimethylsulfoxide [DMSO], 17.5% Cremophor EL, 8.75% Miglyol 810 N, 8.75% ethanol in phosphate buffered saline [PBS]) or in G007-LK enriched chow (100 or 1000 mg G007-LK/kg chow ad libitum, corresponding to a daily G007-LK dose of approximately 20 or 200 mg/kg body mass, respectively, for a mouse with a body mass of 25 g and consumption of approximately 5 g enriched diet/day). G007-LK treatments are initiated at the age of 5 weeks and 5 days for oral gavage treatment or 6 weeks for enriched chow administration and continued for 9 or 21 days, respectively^[2].**

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- **Cancer Discov.** 2019 Oct;9(10):1358-1371.
- **J Mol Med (Berl).** 2019 Aug;97(8):1183-1193.
- **Lab Invest.** 2020 Jan 31.
- **Patent.** US20180263995A1.

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REFERENCES

[1]. Voronkov A, et al. Structural basis and SAR for G007-LK, a lead stage 1,2,4-triazole based specific tankyrase 1/2 inhibitor. *J Med Chem.* 2013 Apr 11;56(7):3012-23.

[2]. Norum JH, et al. The tankyrase inhibitor G007-LK inhibits small intestine LGR5+ stem cell proliferation without altering tissue morphology. *Biol Res.* 2018 Jan 9;51(1):3.

[3]. Xin Chen, et al. Tankyrase inhibitors suppress hepatocellular carcinoma cell growth via modulating the Hippo cascade. *PLoS One.* 2017 Sep 6;12(9):e0184068.

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

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