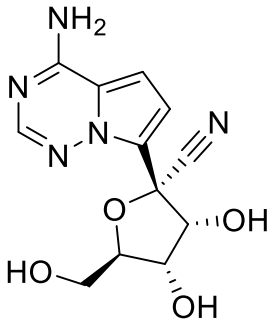
Product data sheet

MedKoo Cat#: 555299 Name: GS-441524 CAS#: 1191237-69-0 (free base) Chemical Formula: $C_{12}H_{13}N_5O_4$ Exact Mass: 291.0968 Molecular Weight: 291.1	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
GS-441524 is a potent inhibitor of feline infectious peritonitis (FIP) virus with an EC50 of 0.78 μM.. GS-441524 strongly inhibits feline infectious peritonitis (FIP) virus in tissue culture and experimental cat infection studies. GS-441524 is a molecular precursor to a pharmacologically active nucleoside triphosphate molecule. These analogs act as an alternative substrate and RNA-chain terminator of viral RNA dependent RNA polymerase. GS-441524 was non-toxic in feline cells at concentrations as high as 100 uM and effectively inhibited FIPV replication in cultured CRFK cells and in naturally infected feline peritoneal macrophages at concentrations as low as 1 uM. Note: GS-441524 is an active metabolite of Remdesivir.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	80.0	274.91

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.44 mL	17.18 mL	34.35 mL
5 mM	0.69 mL	3.44 mL	6.87 mL
10 mM	0.34 mL	1.72 mL	3.44 mL
50 mM	0.07 mL	0.34 mL	0.69 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Murphy BG, Perron M, Murakami E, Bauer K, Park Y, Eckstrand C, Liepnieks M, Pedersen NC. The nucleoside analog GS-441524 strongly inhibits feline infectious peritonitis (FIP) virus in tissue culture and experimental cat infection studies. Vet Microbiol. 2018 Jun;219:226-233. doi: 10.1016/j.vetmic.2018.04.026. Epub 2018 Apr 22. PMID: 29778200; PMCID: PMC7117434.

2. Huang Z, Gong L, Zheng Z, Gao Q, Chen X, Chen Y, Chen X, Xu R, Zheng J, Xu Z, Zhang S, Wang H, Zhang G. GS-441524 inhibits African swine fever virus infection in vitro. Antiviral Res. 2021 May 1;191:105081. doi: 10.1016/j.antiviral.2021.105081. Epub ahead of print. PMID: 33945807.

In vivo study

1. Murphy BG, Perron M, Murakami E, Bauer K, Park Y, Eckstrand C, Liepnieks M, Pedersen NC. The nucleoside analog GS-441524 strongly inhibits feline infectious peritonitis (FIP) virus in tissue culture and experimental cat infection studies. Vet Microbiol. 2018 Jun;219:226-233. doi: 10.1016/j.vetmic.2018.04.026. Epub 2018 Apr 22. PMID: 29778200; PMCID: PMC7117434.

2. Pedersen NC, Perron M, Bannasch M, Montgomery E, Murakami E, Liepnieks M, Liu H. Efficacy and safety of the nucleoside analog GS-441524 for treatment of cats with naturally occurring feline infectious peritonitis. J Feline Med Surg. 2019 Apr;21(4):271-281. doi: 10.1177/1098612X19825701. Epub 2019 Feb 13. PMID: 30755068; PMCID: PMC6435921.

7. Bioactivity

Biological target:

GS-441524, predominant metabolite of Remdesivir and superior to Remdesivir against Covid-19 , shows comparable efficacy in cell-based models of primary human lung and cat cells infected with coronavirus.

In vitro activity

CRFK cells were treated with 100, 33.3, 11.1, 3.7 or 1.2 uM GS-441524 for 24 h. The cells appeared and grew normally at all concentrations of GS-441524 and failed to uptake the fluorescent dye CellTox Green at 24 h (data not shown). The cytotoxic concentration-50% (CC50) was therefore >100 uM. No cytotoxicity (CPE) was observed with CRFK cells exposed to 10 uM of GS-441524 for a longer period of 72 h, either visually or by quantitation of crystal violet staining. It was crucial to show that GS-441524 inhibited FIPV replication in cultured cells at a very low concentration. This was done initially by infecting CRFK cell monolayers with serotype II FIPV-79-1146 and then treating with GS-441524 at concentrations ranging from none to 3.0 uM one hour later. The CRFK cells were protected from virus-induced CPE in a dose-dependent manner when tested 72 h later by crystal violet staining (Fig. 1B). This experiment was repeated three times with similar results and the effective concentration-50% (EC50) of GS-441524 was calculated to be 0.78 uM (Fig. 1C). Inhibition of FIPV replication by GS-441524 was also measured by qRT-RCR in CRFK cells infected with FIPV-79-1146 and exposed one hour later to 50, 10, 1.0, 0.1 and 0 uM GS-441524 for 20 h (Fig. 2 A). Complete inhibition of viral RNA expression was seen at 50 and 10 uM, partial inhibition at 1.0 uM, and no inhibition at lower concentrations ($p < 0.0001$) (Fig. 2A).

Reference: Vet Microbiol. 2018 Jun;219:226-233. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/29778200/

In vivo activity

Twelve adolescent laboratory cats were challenge-exposed to this FIPV and their response to GS-441524 treatment monitored when terminal disease signs became apparent. Ten of 12 of these cats, 16–113, 16-116, 16-119, 16-123 and 124, 16-127 to 131, demonstrated clinical signs consistent with FIP within 10-18 days, while two cats (16-115 and 16-118) remained healthy (Fig. 3). Clinical signs of FIP in the affected cats started with hyperthermia (>103 F) (Fig. 4) and lymphopenia (less than or equal to 1700 cells/ul blood) (Fig. 5), and then rapidly progressed to depression, anorexia, hyperbilirubinemia, and ascites. The severity of lymphopenia appeared to be proportional to the severity of overall disease signs and one cat (16–113) had a measured nadir of 143 lymphocytes/ul blood (Fig. 5). Rectal temperature and lymphocyte levels remained normal in the two asymptomatic cats. The 10 cats that developed disease signs were divided into two groups and treated with either 5 mg/kg (Group A; n = 5) or 2 mg/kg (Group B; n = 5) GS-441524 SC q24 h starting three days after unequivocal clinical evidence of FIP (days 12–19 post infection) (Fig. 3, Fig. 4, Fig. 5). The two cats that did not develop disease signs served as controls for normal blood lymphocyte counts and rectal temperature. All 10 treated cats had a rapid response to treatment and lymphocyte levels and rectal temperatures returned to pre-infection levels and levels of the two asymptomatic cats (Figs. 4,5). Two of the 10 treated cats, 16–116 (Group A) and 16–127 (Group B), had recurrences disease at four and six weeks post treatment (Fig. 3). These two cats were treated a second time for two weeks and their response was identical to that of primary treatment (data not shown). All ten of the once or twice treated cats have remained normal to date (more than eight months post infection). No significant signs of toxicity were noted during or after primary or secondary treatment. Injections caused a transient "stinging" reaction in some cats within 10 s of compound administration. Localized and transient pain was evidenced by unusual posturing, licking at the injection site and/or vocalizations that lasted for approximately 30–60 s after injection. Injection reactions were more pronounced in some animals relative to others and reactions were inconsistent from one injection to the next and decreased over time.

Reference: Vet Microbiol. 2018 Jun;219:226-233. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/29778200/